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                  with preparation role
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                  to 50,000
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 NEWS 15  JAN 29  CAS Registry Number crossover limit increased to 300,000 in
                  multiple databases
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 NEWS 17  FEB 15  RUSSIAPAT enhanced with pre-1994 records
 NEWS 18  FEB 23  KOREAPAT enhanced with IPC 8 features and functionality
 NEWS 19  FEB 26  MEDLINE reloaded with enhancements
 NEWS 20  FEB 26  EMBASE enhanced with Clinical Trial Number field
 NEWS 21  FEB 26  TOXCENTER enhanced with reloaded MEDLINE
 NEWS 22  FEB 26  IFICDB/IFIPAT/IFIUDB reloaded with enhancements
 NEWS 23  FEB 26  CAS Registry Number crossover limit increased from 10,000
                  to 300,000 in multiple databases
 NEWS 24  MAR 15  WPIDS/WPIX enhanced with new FRAGHITSTR display format
 NEWS 25  MAR 16  CASREACT coverage extended
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L2          248 L1 AND PROTEOL?

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L3          142 DUP REM L2 (106 DUPLICATES REMOVED)

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L3   ANSWER 1 OF 142  CAPLUS  COPYRIGHT 2007 ACS on STN DUPLICATE 1
TI   Mechanism of apoptosis induced by IFN-α in human myeloma cells: Role
     of Jak1 and Bim and potentiation by rapamycin

L3   ANSWER 2 OF 142  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on
     STN                                                 DUPLICATE 2
TI   Adenoviral-mediated interferon a overcomes resistance to the interferon
     protein in various cancer types and has marked bystander effects.

L3   ANSWER 3 OF 142  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Methods for individually optimizing treatment for an inflammation-
     associated disease

L3   ANSWER 4 OF 142  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Use of gene expression data and other biochemical criteria in predicting
     responsiveness to chemotherapy in breast cancer patients

L3   ANSWER 5 OF 142  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Use of fusion proteins that can be taken up by skin cells to deliver
     therapeutic macromolecules to the bloodstream without injection
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L3 ANSWER 6 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Method for treating dementia or alzheimer's disease using a CD20 antibody

L3 ANSWER 7 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Genes showing altered levels of expression in pancreatic disease and their use in diagnosis and prognosis of pancreatic cancer

L3 ANSWER 8 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Vaccinia virus infection attenuates innate immune responses and antigen presentation by epidermal dendritic cells

L3 ANSWER 9 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Viral and therapeutic control of IFN-beta promoter stimulator 1 during hepatitis C virus infection.

L3 ANSWER 10 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Chloroquine possesses a potent inhibitory effect of replication of HCV replicon.

L3 ANSWER 11 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI The C-terminal 26-residue peptide of serpin A1 is an inhibitor of HIV-1.

L3 ANSWER 12 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Differential gene induction by type I and type II Interferons and their combination.

L3 ANSWER 13 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Strategies to improve plasma half life time of peptide and protein drugs

L3 ANSWER 14 OF 142 MEDLINE on STN
TI Hepatitis C virus NS2 and NS3/4A proteins are potent inhibitors of host cell cytokine/chemokine gene expression.

L3 ANSWER 15 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 3
TI Induction of APOBEC3 family proteins, a defensive maneuver underlying interferon-induced anti-HIV-1 activity.

L3 ANSWER 16 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 4
TI TYK2 activity promotes ligand-induced IFNAR1 proteolysis.

L3 ANSWER 17 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Multiple sclerosis and virus induced immune responses: Autoimmunity can be primed by molecular mimicry and augmented by bystander activation.

L3 ANSWER 18 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Prospects of formulating proteins/peptides as aerosols for pulmonary drug delivery.

L3 ANSWER 19 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Hepatitis C virus NS2 and NS3/4A proteins are potent inhibitors of host cell cytokine/chemokine gene expression

L3 ANSWER 20 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Truncated sialyltransferase ST6GalNAc I polypeptides and nucleic acids

L3 ANSWER 21 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Truncated polypeptide N-acetylgalactosaminyltransferase II polypeptides and nucleic acids

L3 ANSWER 22 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Differentially expressed gene profile for diagnosing and treating mental disorders

L3 ANSWER 23 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Interferon Induces NF-κB-inducing Kinase/Tumor Necrosis Factor Receptor-associated Factor-dependent NF-κB Activation to Promote Cell Survival

L3 ANSWER 24 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 5
TI Crystal structure of the interferon-induced ubiquitin-like protein ISG15.

L3 ANSWER 25 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI High Serum Levels of Matrix Metalloproteinase-9 and Matrix Metalloproteinase-1 Are Associated with Rapid Progression in Patients with Metastatic Melanoma

L3 ANSWER 26 OF 142 MEDLINE on STN
TI Enhancement of dendritic cell antigen cross-presentation by CpG DNA involves type I IFN and stabilization of class I MHC mRNA.

L3 ANSWER 27 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 6
TI Engineering glycoprotein B of bovine herpesvirus 1 to function as transporter for secreted proteins: a new protein expression approach.

L3 ANSWER 28 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 7
TI Intracellular domain of the IFNaR2 interferon receptor subunit mediates transcription via Stat2.

L3 ANSWER 29 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Regulated intramembrane proteolysis signaling by an interferon receptor.

L3 ANSWER 30 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 8
TI TGF-beta 1 mRNA expression in liver biopsy specimens and TGF-beta 1 serum levels in patients with chronic hepatitis C before and after antiviral therapy.

L3 ANSWER 31 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 9
TI Interferons induce proteolytic degradation of TRAILR4.

L3 ANSWER 32 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Involvement of PKR and RNase L in translational control and induction of apoptosis after Hepatitis C polyprotein expression from a vaccinia virus recombinant

L3 ANSWER 33 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 10
TI Gene expression profiles and biomarkers for the detection of Chagas disease and other disease-related gene transcripts in blood

L3 ANSWER 34 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 11

TI Gene expression profiles and biomarkers for the detection of lung disease-related and other disease-related gene transcripts in blood

L3 ANSWER 35 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Transit peptide cleavage site sequences for production of plastid-targeted fusion proteins in plant cells

L3 ANSWER 36 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Cell surface polypeptides from Lactobacillus or Bifidobacterium and their use as immunomodulating probiotic compounds

L3 ANSWER 37 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Gene expression profile of human and mouse genes in atopic dermatitis and psoriasis patients and its use for diagnosis, therapy, and drug screening

L3 ANSWER 38 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI High throughput directed evolution of proteins and peptides using two-dimensional rational mutagenesis scanning

L3 ANSWER 39 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Sequences of human schizophrenia related genes and use for diagnosis, prognosis and therapy

L3 ANSWER 40 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Gann Monograph on Cancer Research:SPECIAL ISSUE IN COMMEMORATION OF THE 100TH ANNIVERSARY OF THE LATE DR. TOMIZO YOSHIDA'S BIRTH.

L3 ANSWER 41 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 12
TI Regulated proteolysis of the IFNaR2 subunit of the interferon-alpha receptor.

L3 ANSWER 42 OF 142 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
TI [Soluble transferrin receptor concentration, interleukin 6 and 12 levels, alanine aminotransferase activity and viral load in children with chronic hepatitis C treated with interferon and ribavirine]. STEZENIE ROZPUSZCZALNEGO RECEPTORA TRANSFERYNY, POZIOM INTERLEUKINY 6 I 12, AKTYWNOSC AMINOTRANSFERAZY ALANINOWEJ ORAZ WIREMIA U DZIECI Z PRZEWLEKLYM ZAPALENIEM WATROBY TYPU C LECZONYCH INTERFERONEM I RYBAWIRYNA.

L3 ANSWER 43 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Diversity and Relatedness Among the Type I Interferons

L3 ANSWER 44 OF 142 MEDLINE on STN
TI Interferon therapy in chronic myelogenous leukemia.

L3 ANSWER 45 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 13
TI Undermining tumor angiogenesis by gene therapy: An emerging field

L3 ANSWER 46 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 14
TI A reporter-based assay for identifying hepatitis C virus inhibitors based on subgenomic replicon cells

L3 ANSWER 47 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI An interferon receptor signals via regulated intramembrane proteolysis (RIP).

L3 ANSWER 48 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Ligand binding domains of cytokine which are linked via flexible

polypeptide linker and uses in therapy

L3 ANSWER 49 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 15
TI SCFHOS ubiquitin ligase mediates the ligand-induced down-regulation of the interferon-alpha receptor.

L3 ANSWER 50 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 16
TI Tissue remodelling in liver diseases.

L3 ANSWER 51 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Regulation of the expression and processing of caspase-12.

L3 ANSWER 52 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Development of a cell-based assay for monitoring specific hepatitis C virus NS3/4A protease activity in mammalian cells

L3 ANSWER 53 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Pathological mechanisms associated with CD34+ cell mobilization in idiopathic myelofibrosis.

L3 ANSWER 54 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Adhesion protein, protease, and protease inhibitor mutations and methods for diagnosis and treatment of epithelial cell adhesion-associated diseases

L3 ANSWER 55 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Long-acting cytokine derivatives and their pharmaceutical compositions

L3 ANSWER 56 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI In situ Langerhans cell vaccine

L3 ANSWER 57 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Therapeutic modulation of the tumor inflammatory response

L3 ANSWER 58 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes

L3 ANSWER 59 OF 142 MEDLINE on STN
TI Selective STAT protein degradation induced by paramyxoviruses requires both STAT1 and STAT2 but is independent of alpha/beta interferon signal transduction.

L3 ANSWER 60 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 17
TI Microwave-enhanced enzyme reaction for protein mapping by mass spectrometry: A new approach to protein digestion in minutes.

L3 ANSWER 61 OF 142 MEDLINE on STN
TI High expression levels of collagenase-1 and stromelysin-1 correlate with shorter disease-free survival in human metastatic melanoma.

L3 ANSWER 62 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Modulation of monocytes matrix metalloproteinase-2, MT1-MMP and TIMP-2 by interferon-alpha and -beta: Implications to multiple sclerosis.

L3 ANSWER 63 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 18
TI Secretion of human interferon alpha 2b by Streptomyces lividans.

L3 ANSWER 64 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 19
TI The nonstructural NS5A protein of hepatitis C virus: An expanding, multifunctional role in enhancing hepatitis C virus pathogenesis.

L3 ANSWER 65 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Proteolytic degradation of the recombinant target protein, interferon-τ during its fermentative production in the methylotrophic yeast, Pichia pastoris

L3 ANSWER 66 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 20
TI Production of IFNalpha-2a in Hansenula polymorpha.

L3 ANSWER 67 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Post-translational modification of recombinant proteins in plants by altering its natural modification abilities

L3 ANSWER 68 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 21
TI Prolonging the half-life of human interferon-alpha2 in circulation: Design, preparation, and analysis of (2-sulfo-9-fluorenylmethoxycarbonyl)7-interferon-alpha2.

L3 ANSWER 69 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 22
TI Virus infection induces proteolytic processing of IL-18 in human macrophages via caspase-1 and caspase-3 activation

L3 ANSWER 70 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Angiogenesis: Regulators and clinical applications.

L3 ANSWER 71 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI The V Protein of Human Parainfluenza Virus 2 Antagonizes Type I Interferon Responses by Destabilizing Signal Transducer and Activator of Transcription 2

L3 ANSWER 72 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Systems for oral delivery

L3 ANSWER 73 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of recombinant interferon-α lacking methionine residue at N-terminal

L3 ANSWER 74 OF 142 MEDLINE on STN
TI Activity of growth factors in the IL-6 group in the differentiation of human lung adenocarcinoma.

L3 ANSWER 75 OF 142 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
TI Adoptive transfer from interferon-α -fed mice is associated with inhibition of active experimental autoimmune encephalomyelitis by decreasing recipient tumor necrosis factor-α secretion.

L3 ANSWER 76 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 23

TI Expression of Flt3-ligand by the endothelial cell.

L3 ANSWER 77 OF 142 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
TI Combination therapy with glatiramer acetate (copolymer-1) and a type I interferon (IFN-α) does not improve experimental autoimmune encephalomyelitis.

L3 ANSWER 78 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Gene probes used for genetic profiling in healthcare screening and planning

L3 ANSWER 79 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Gene probes used for genetic profiling in healthcare screening and planning

L3 ANSWER 80 OF 142 MEDLINE on STN
TI A dynamic connection between centromeres and ND10 proteins.

L3 ANSWER 81 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Inflammatory mediators regulate cathepsin S in macrophages and microglia: a role in attenuating heparan sulfate interactions

L3 ANSWER 82 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 24
TI Hybrid (BDBB) interferon-alpha: Preformulation studies.

L3 ANSWER 83 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Therapeutic intervention with complement and β-glucan in cancer

L3 ANSWER 84 OF 142 MEDLINE on STN
TI Tumour response and radiation-induced lung injury in patients with recurrent small cell lung cancer treated with radiotherapy and concomitant interferon-alpha.

L3 ANSWER 85 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 25
TI Identification of a linear epitope of interferon-alpha2b recognized by neutralizing monoclonal antibodies.

L3 ANSWER 86 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Protein-lipid vesicles and autogenous vaccine comprising the same

L3 ANSWER 87 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Cloning and cDNA sequences of human interferon .alpha ./β-binding proteins I and II and their pharmaceutical uses

L3 ANSWER 88 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 26
TI Effects of IFNalpha on late stages of HIV-1 replication cycle.

L3 ANSWER 89 OF 142 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN DUPLICATE 27
TI Glucocorticoids and Th-1, Th-2 type cytokines in rheumatoid arthritis, osteoarthritis, asthma, atopic dermatitis and AIDS.

L3 ANSWER 90 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 28
TI The use of Wobenzym to facilitate interferon synthesis in the treatment of chronic urogenital chlamydiosis.

L3 ANSWER 91 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 29
TI Modulation of Apo-1/Fas (CD95)-induced programmed cell death in myeloma cells by interferon-alpha-2.

L3 ANSWER 92 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Conjugation of the 15-kDa interferon-induced ubiquitin homolog is distinct from that of ubiquitin

L3 ANSWER 93 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Interferon-alpha/beta binding protein, its preparation and use

L3 ANSWER 94 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 30
TI The cytokines of inflammation.

L3 ANSWER 95 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 31
TI Interferon-alpha-2b increases fibrolysis in fibrotic livers from bile duct ligated rats: Possible participation of the plasminogen activator.

L3 ANSWER 96 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Interferon increases extracellular matrix degradation and plasminogen activator activity in livers from cirrhotic rats.

L3 ANSWER 97 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Resistance of recombinant proteins to proteolysis during folding and in the folded state

L3 ANSWER 98 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Lipopolysaccharide (LPS), LPS-immune complexes and cytokines as inducers of pulmonary inflammation in patients with cystic fibrosis and chronic Pseudomonas aeruginosa lung infection.

L3 ANSWER 99 OF 142 MEDLINE on STN
TI Approaches to the development of novel inhibitors of hepatitis C virus replication.

L3 ANSWER 100 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 32
TI Modulation of THE bovine microvascular endothelial cell proteolytic properties by inhibitors of angiogenesis.

L3 ANSWER 101 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 33
TI Proteolytic enzymes and amylase induce cytokine production in human peripheral blood mononuclear cells in vitro.

L3 ANSWER 102 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 34
TI Interferon-alpha-2 counteracts interleukin-1-alpha-stimulated expression of urokinase-type plasminogen activator in human foreskin microvascular endothelial cells in vitro.

L3 ANSWER 103 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Quantitation of interferon-induced Mx protein in whole blood lysates by an immunochemiluminescent assay: elimination of protease activity of cell lysates in toto

L3 ANSWER 104 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 35
TI Alpha- and gamma-interferon inhibit plasminogen activator inhibitor-1 gene expression in human retinal pigment epithelial cells

L3 ANSWER 105 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 36
TI Expression of human interferon-alpha-2 in Sf9 cells. Characterization of O-linked glycosylation and protein heterogeneities.

L3 ANSWER 106 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Cytokine synthesis in human peripheral blood mononuclear cells after oral administration of polyenzyme preparations

L3 ANSWER 107 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI The human gene encoding tryptophanyl-tRNA synthetase: interferon-response elements and exon-intron organization

L3 ANSWER 108 OF 142 MEDLINE on STN
TI Soluble tumor necrosis factor receptor expression in patients with metastatic renal cell carcinoma treated with interleukin-2-based immunotherapy.

L3 ANSWER 109 OF 142 MEDLINE on STN
TI Tumor necrosis factor induction of endothelial cell urokinase-type plasminogen activator mediated proteolysis of extracellular matrix and its antagonism by gamma-interferon.

L3 ANSWER 110 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Nerve lesions induced by macrophage activation.

L3 ANSWER 111 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Regulation of Staphylococcus protease using complement, interferon and immunoglobulin as substrates

L3 ANSWER 112 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI [Ala IL-8] as a leukocyte adhesion inhibitor, and its recombinant production, purification, and activity

L3 ANSWER 113 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Chemically synthesized gene provides in Escherichia coli cells for the biosynthesis of a polypeptide, the structure of which corresponds to human α2 leukocyte interferon

L3 ANSWER 114 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 37
TI NATURAL HUMAN INTERFERON-ALPHA-2 IS O-GLYCOSYLATED.

L3 ANSWER 115 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 38
TI Mapping of an epitope of human leukocyte α interferon A which is recognized by the murine monoclonal antibody NK2

L3 ANSWER 116 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Structural analysis of recombinant proteins by fast atom bombardment and californium-252 plasma desorption mass spectrometry

L3 ANSWER 117 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Charge heterogeneity of β2-microglobulin in lymphoid cells

L3 ANSWER 118 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Structural organization of the interferon molecules as precursors of

immuno- and neuroactive oligopeptides

L3 ANSWER 119 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 39
TI SECRETORY EXPRESSION IN ESCHERICHIA-COLI AND BACILLUS-SUBTILIS OF HUMAN INTERFERON ALPHA GENES DIRECTED BY STAPHYLOKINASE SIGNALS.

L3 ANSWER 120 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 40
TI CELL SURFACE-ASSOCIATED PROTEINASES IN NK CELL-MEDIATED CYTOTOXICITY ENHANCEMENT OF ENZYME EXPRESSION IS UNIQUE TO ACTIVATION WITH INTERFERON-ALPHA.

L3 ANSWER 121 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Lymphocytes treated with natural alpha-interferon produce a chemotactic factor for human neutrophils

L3 ANSWER 122 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 41
TI LOW TEMPERATURES STABILIZE INTERFERON ALPHA-2 AGAINST PROTEOLYSIS IN METHYLOPHILUS-METHYLOTROPHUS AND ESCHERICHIA-COLI.

L3 ANSWER 123 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 42
TI ACTIVATION OF PROTEIN BREAKDOWN AND PROSTAGLANDIN E-2 PRODUCTION IN RAT SKELETAL MUSCLE IN FEVER IS SIGNALED BY A MACROPHAGE PRODUCT DISTINCT FROM INTERLEUKIN 1 OR OTHER KNOWN MONOKINES.

L3 ANSWER 124 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 43
TI STUDY OF OLIGOMERIC FORMS OF HUMAN LEUKOCYTE INTERFERONS OBTAINED BY GENE ENGINEERING TECHNIQUES.

L3 ANSWER 125 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Identification and partial characterization of a novel protease in Saccharomyces cerevisiae which cleaves the peptide bond between residues 22 and 23 in α-interferon, and identification of an α-interferon resistant to said proteolysis

L3 ANSWER 126 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Chemical characterization of recombinant human leukocyte interferon A using fast atom bombardment mass spectrometry

L3 ANSWER 127 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI INFLUENCE OF ENERGY SOURCE AND HEAT ON THE STABILITY OF HUMAN INTERFERON ALPHA-2 IN METHYLOPHILUS-METHYLOTROPHUS.

L3 ANSWER 128 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 44
TI PROTEOLYSIS IN THE OBLIGATE METHYLOTROPH METHYLOPHILUS-METHYLOTROPHUS.

L3 ANSWER 129 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 45
TI INTRACELLULAR DEGRADATION OF RECOMBINANT PROTEINS IN RELATION TO THEIR LOCATION IN ESCHERICHIA-COLI CELLS.

L3 ANSWER 130 OF 142 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
TI 7. Isolation and purification of human alpha interferon, a recombinant DNA

protein.

L3 ANSWER 131 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI High-performance liquid chromatography analysis of recombinant interferon-α 2 and interferon-.
alpha.2 analogue proteins purified by immunoabsorption chromatography

L3 ANSWER 132 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Interferon secreted by Bacillus subtilis is retained by membranes

L3 ANSWER 133 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Chromatographic methods for purification of leukocyte interferon

L3 ANSWER 134 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Modified (1-28) beta interferons

L3 ANSWER 135 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 46
TI COMPARATIVE IMMUNOCHEMICAL STUDY OF SOME HUMAN LEUKOCYTE INTERFERONS.

L3 ANSWER 136 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 47
TI LIMITED PROTEOLYSIS OF HUMAN LEUKOCYTE INTERFERON ALPHA-2 AND LOCALIZATION OF THE MONOCLONAL ANTIBODY BINDING ANTIGENIC DETERMINANT.

L3 ANSWER 137 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Secretion of foreign proteins from Saccharomyces cerevisiae directed by α-factor gene fusions

L3 ANSWER 138 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 48
TI BIOLOGIC ACTIVITY IN A FRAGMENT OF RECOMBINANT HUMAN INTERFERON ALPHA.

L3 ANSWER 139 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Mouse interferon receptors: a difference in their response to α and β interferons

L3 ANSWER 140 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 49
TI Interferon-mediated inhibition of production of Gazdar murine sarcoma virus, a retrovirus lacking env proteins and containing an uncleaved gag precursor

L3 ANSWER 141 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI A new mass-spectrometric C-terminal sequencing technique finds a similarity between γ-interferon and α2-interferon and identifies a proteolytically clipped γ-interferon that retains full antiviral activity

L3 ANSWER 142 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI The kidney is the main site of interferon degradation

=> Log off H
SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 13:42:49 ON 25 MAR 2007

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PASSWORD:
 * * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE'
AT 13:56:52 ON 25 MAR 2007
FILE 'BIOSIS' ENTERED AT 13:56:52 ON 25 MAR 2007
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FILE 'MEDLINE' ENTERED AT 13:56:52 ON 25 MAR 2007

COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                               50.90      51.11

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     (FILE 'HOME' ENTERED AT 13:34:30 ON 25 MAR 2007)

     FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE' ENTERED AT 13:34:48 ON 25 MAR 2007
L1        70256 S (INTERFERON ALPHA) OR IFN-ALPHA AND (MUTEIN OR VARIANT OR MUT
L2          248 S L1 AND PROTEOL?
L3          142 DUP REM L2 (106 DUPLICATES REMOVED)

=> S L3 and Resistance
L4          21 L3 AND RESISTANCE

=> D Ti L4 1-24

L4   ANSWER 1 OF 21  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
TI   Adenoviral-mediated interferon a overcomes resistance to the
     interferon protein in various cancer types and has marked bystander
     effects.

L4   ANSWER 2 OF 21  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
TI   Gann Monograph on Cancer Research:SPECIAL ISSUE IN COMMEMORATION OF THE
     100TH ANNIVERSARY OF THE LATE DR. TOMIZO YOSHIDA'S BIRTH.

L4   ANSWER 3 OF 21  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Use of gene expression data and other biochemical criteria in predicting
     responsiveness to chemotherapy in breast cancer patients

L4   ANSWER 4 OF 21  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Genes showing altered levels of expression in pancreatic disease and their
     use in diagnosis and prognosis of pancreatic cancer

L4   ANSWER 5 OF 21  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Truncated polypeptide N-acetylgalactosaminyltransferase II polypeptides
     and nucleic acids

L4   ANSWER 6 OF 21  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Truncated sialyltransferase ST6GalNAc I polypeptides and nucleic acids

L4   ANSWER 7 OF 21  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Differentially expressed gene profile for diagnosing and treating mental
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disorders

L4 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
TI Sequences of human schizophrenia related genes and use for diagnosis, prognosis and therapy

L4 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
TI Gene expression profiles and biomarkers for the detection of Chagas disease and other disease-related gene transcripts in blood

L4 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
TI Gene expression profile of human and mouse genes in atopic dermatitis and psoriasis patients and its use for diagnosis, therapy, and drug screening

L4 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
TI High throughput directed evolution of proteins and peptides using two-dimensional rational mutagenesis scanning

L4 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
TI Ligand binding domains of cytokine which are linked via flexible polypeptide linker and uses in therapy

L4 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
TI Endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes

L4 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
TI Long-acting cytokine derivatives and their pharmaceutical compositions

L4 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
TI Gene probes used for genetic profiling in healthcare screening and planning

L4 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
TI Gene probes used for genetic profiling in healthcare screening and planning

L4 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
TI Therapeutic intervention with complement and β-glucan in cancer

L4 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
TI Cloning and cDNA sequences of human interferon .alpha ./β-binding proteins I and II and their pharmaceutical uses

L4 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
TI Interferon-alpha/beta binding protein, its preparation and use

L4 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
TI Resistance of recombinant proteins to proteolysis during folding and in the folded state

L4 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
TI Identification and partial characterization of a novel protease in Saccharomyces cerevisiae which cleaves the peptide bond between residues 22 and 23 in α-interferon, and identification of an α-interferon resistant to said proteolysis

=> D Ibib ABS L4 1-21

L4 ANSWER 1 OF 21 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2007:206271 BIOSIS
DOCUMENT NUMBER: PREV200700198033
TITLE: Adenoviral-mediated interferon a overcomes resistance to the interferon protein in various cancer types and has marked bystander effects.
AUTHOR(S): Zhang, X.; Yang, Z.; Dong, L.; Papageorgiou, A.; McConkey, D. J.; Benedict, W. F. [Reprint Author]
CORPORATE SOURCE: Univ Texas, MD Anderson Canc Ctr, Dept Genitourinary Med Oncol, 1515 Holcombe Blvd,Box 1374, Houston, TX 77030 USA wbenedic@mdanderson.org
SOURCE: Cancer Gene Therapy, (MAR 2007) Vol. 14, No. 3, pp. 241-250.
ISSN: 0929-1903.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Mar 2007
Last Updated on STN: 21 Mar 2007

AB We have previously shown that intravesical administration of adenovirus encoding human interferon alpha-2b (Ad-IFN) induced a marked regression of superficial human bladder tumors derived from cells that are resistant to over 1 million units/ml of IFN alpha protein in vitro. In addition, Ad-IFN appeared to produce strong bystander effects. In this study, we show that Ad-IFN causes marked inhibition of cell growth and apoptosis in cells of various tumor types, all of which are resistant to IFN alpha protein. In addition, strong perinuclear IFN staining was seen in all cell lines following Ad-IFN transfection and was never observed after exposure to the IFN protein. Ad-IFN induced proteolytic processing of caspases 3, 8 and 9, indicative of enzymatic activation. However, the caspase-8-selective inhibitor, IETDfmk, blocked apoptosis only in the cell lines that were sensitive to the IFN alpha protein and had minimal effect on Ad-IFN-induced caspase-3 or -9 processing and cell death, indicating that death receptor-independent mechanism(s) were involved in the cytotoxic effects observed for cancer cell lines resistant to the IFN alpha protein. Moreover, we document that a yet to be identified soluble factor(s) is responsible for causing the bystander effect observed following Ad-IFN treatment in IFN protein-resistant cancer cells.

L4 ANSWER 2 OF 21 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:165130 BIOSIS
DOCUMENT NUMBER: PREV200600160152
TITLE: Gann Monograph on Cancer Research:SPECIAL ISSUE IN COMMEMORATION OF THE 100TH ANNIVERSARY OF THE LATE DR. TOMIZO YOSHIDA'S BIRTH.
AUTHOR(S): Tsuruo, T [Editor]; Kitagawa, T [Editor]
SOURCE: Tsuruo, T [Editor]; Kitagawa, T [Editor]. Gann Monograph on Cancer Research, (2004) Gann Monograph on Cancer Research:SPECIAL ISSUE IN COMMEMORATION OF THE 100TH ANNIVERSARY OF THE LATE DR. TOMIZO YOSHIDA'S BIRTH. Publisher: JAPAN SCIENTIFIC SOC PRESS, 2-10 HONGO, 6-CHOME, BUNKYO-KU, TOKYO, 113, JAPAN. Series: GANN MONOGRAPH ON CANCER RESEARCH.
ISSN: 0072-0151. ISBN: 3-8055-7816-4(H).
DOCUMENT TYPE: Book
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Mar 2006
Last Updated on STN: 9 Mar 2006

AB This 280-page book, entitled 'Cancer Research Front of Japan, 2003' is volume 52 of the Gann Monograph on Cancer Research Series and is a special issue published in commemoration of the late Dr. Tomizo Yoshida's birth, who initiated the first publication of this series in 1966. This volume is structured into 4 major sections and contains 18 individually-authored

papers. The focus of the first section is pathology and there are 4 papers in this section that individually discuss: the isolation of p53-target genes and their functional analysis; cell adhesion system and human cancer morphogenesis; gastrointestinal stromal tumor as a model for molecular-based diagnosis and treatment of solid tumors; and stem cells and gastric cancer and the role of gastric and intestinal mixed intestinal metaplasia. Carcinogenesis is the theme of the second section, which contains 4 more specific papers. Topics covered in these 4 papers include: renal carcinogenesis in terms of genotype, phenotype and dramatype; heterocyclic amines as mutagens/carcinogens produced during the cooking of meat and fish; a medium-term rat liver bioassay for rapid in vivo detection of the carcinogenic potential of chemicals; and the metabolic activation of polycyclic aromatic hydrocarbons to carcinogens by cytochromes P450 1A1 and 1B1. Cell biology is the focus of the third section, which contains 6 papers on the topic. These 6 papers individually discuss: NK4 in cancer biology and therapeutics; new aspects of interferon-alpha/beta (IFN-alpha/beta) signaling in immunity, oncogenesis and bone metabolism; tumor formation by genetic mutations of beta-catenin, APC, and axin in the Wnt signaling pathway; regulation of transforming growth factor-beta (TGF-beta) signaling and its roles in tumor progression; vascular endothelial growth factor (VEGF) receptor-2 and its unique signaling and specific ligand, VEGF-2; and the roles of pericellular proteolysis by membrane type-1 matrix metalloproteinase in cancer invasion and angiogenesis. The final section concentrates on chemotherapy and the 4 papers in this section individually discuss the antitumor activity of sugar-modified cytosine nucleosides; molecular targeting therapy of cancer in terms of drug resistance , apoptosis and survival signal; the basic and clinical implications of ABC transporters, Y-box-binding protein-1 (YB-1) and angiogenesis-related factors in human malignancies; and molecular mechanisms of angiogenesis in non-small cell lung cancer, and therapeutics targeting related molecules. The book is indexed by author and by subject, and contains 59 figures, 18 of which are in color, and 16 tables. This book will be of interest to oncologists, tumor biology researchers, cell biologists, toxicologists, pathologists and pharmacologists.

L4 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:795782 CAPLUS
DOCUMENT NUMBER: 145:208138
TITLE: Use of gene expression data and other biochemical criteria in predicting responsiveness to chemotherapy in breast cancer patients
INVENTOR(S): Dai, Hongyue; Friend, Stephen H.; Deutsch, Paul
PATENT ASSIGNEE(S): Rosetta Inpharmatics LLC, USA; Merck & Co., Inc.
SOURCE: PCT Int. Appl., 349pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006084272	A2	20060810	WO 2006-US4280	20060206

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,

IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-650365P P 20050204

AB A method of predicting the responsiveness of a breast cancer patient to chemotherapy using a combination of biochem. criteria, especially estrogen receptor levels, age, and gene expression profiles is described. The invention also provides a method for selecting patients for enrollment in a clin. trial of a drug for treating breast cancer based on these factors. Methods of statistical anal. and integration of these data are described.

L4 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:238155 CAPLUS
DOCUMENT NUMBER: 144:310062
TITLE: Genes showing altered levels of expression in pancreatic disease and their use in diagnosis and prognosis of pancreatic cancer
INVENTOR(S): Kloeppel, Guenter; Luettges, Jutta; Kalthoff, Holger; Ammerpohl, Ole; Gruetzmann, Robert; Pilarsky, Christian; Saeger, Hans Detlev; Alldinger, Ingo
PATENT ASSIGNEE(S): Technische Universitaet Dresden, Germany
SOURCE: Ger. Offen., 132 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 102004042822	A1	20060316	DE 2004-102004042822	20040831
WO 2006024283	A2	20060309	WO 2005-DE1527	20050826
WO 2006024283	A3	20060831		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: DE 2004-102004042822A 20040831

AB Genes showing altered levels of expression in healthy vs. neoplastic pancreas are identified for use in the diagnosis of cancers including ductal adenocarcinoma; as indicators in screening for effective drugs; and as targets for nucleic acid-based therapies including antisense nucleic acids or siRNA. Gene expression profiling identified 1419 genes showing changes in levels of expression in neoplastic epithelium of which 650 were up-regulated and 769 were down-regulated. Of the 1419 genes, 1267 were not previously known to have any connection with pancreatic neoplasms.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1330475 CAPLUS
DOCUMENT NUMBER: 144:65957
TITLE: Truncated polypeptide N-acetylgalactosaminyltransferas

e II polypeptides and nucleic acids
INVENTOR(S): Johnson, Karl F.; Chen, Xi; Taudte, Susann; Saribas, Sami
PATENT ASSIGNEE(S): Neose Technologies, Inc., USA
SOURCE: PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005121331	A2	20051222	WO 2005-US19442	20050603
WO 2005121331	A8	20060309		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-546530P P 20040603
US 2004-598584P P 20040803

AB The present invention features compns. and methods related to mutants of human polypeptide N-acetylgalactosaminyltransferase II (GalNAcT2) that are truncated by deletion of the N-terminal 1-40, 1-73, or 1-94 residues. Truncated forms of GalNAcT2 possess biol. activities comparable to, and in some instances, in excess of their full-length polypeptide counterparts, and may have enhanced properties of solubility, stability, and resistance to proteolytic degradation GalNAcT2 is an essential reagent for glycosylation of therapeutic glycopeptides and oligosaccharides. The invention also features nucleic acids encoding such truncated polypeptides, as well as vectors, host cells, expression systems, and methods of expressing and using such polypeptides.

L4 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1330319 CAPLUS
DOCUMENT NUMBER: 144:65956
TITLE: Truncated sialyltransferase ST6GalNAc I polypeptides and nucleic acids
INVENTOR(S): Johnson, Karl F.; Hakes, David; Wei, Ge; Liu, Li; Saribas, Sami; Sjoberg, Eric; Clausen, Henrik; Bennett, Eric Paul; Mobasseri, Aliakbar
PATENT ASSIGNEE(S): Neose Technologies, Inc., USA
SOURCE: PCT Int. Appl., 192 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005121332	A2	20051222	WO 2005-US19583	20050603

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-576433P P 20040603
US 2005-650011P P 20050204

AB The present invention features compns. and methods related to mutants of human, murine, and chicken CMP-acetylneuraminate-α-acetylgalactosaminide α2-6-sialyltransferase (ST6GalNAcI) that are truncated by deletion of N-terminal residues. Truncated forms of ST6GalNAcI possess biol. activities comparable to, and in some instances, in excess of their full-length polypeptide counterparts, and may have enhanced properties of solubility, stability, and resistance to proteolytic degradation ST6GalNAcI is an essential reagent for glycosylation of therapeutic glycopeptides and oligosaccharides. The invention also features nucleic acids encoding such truncated polypeptides, as well as vectors, host cells, expression systems, and methods of expressing and using such polypeptides.

L4 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:447673 CAPLUS
DOCUMENT NUMBER: 143:20875
TITLE: Differentially expressed gene profile for diagnosing and treating mental disorders
INVENTOR(S): Akil, Huda; Atz, Mary; Bunney, William E., Jr.; Choudary, Prabhakara V.; Evans, Simon J.; Jones, Edward G.; Li, Jun; Lopez, Juan F.; Myers, Richard; Thompson, Robert C.; Tomita, Hiroaki; Vawter, Marquis P.; Watson, Stanley
PATENT ASSIGNEE(S): The Board of Trustees of the Leland Stanford Junior University, USA
SOURCE: PCT Int. Appl., 226 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005046434	A2	20050526	WO 2004-US36784	20041105
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005209181	A1	20050922	US 2004-982556	20041104
AU 2004289247	A1	20050526	AU 2004-289247	20041105
CA 2543811	A1	20050526	CA 2004-2543811	20041105
EP 1680009	A2	20060719	EP 2004-800741	20041105

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU

PRIORITY APPLN. INFO.: US 2003-517751P P 20031105
US 2004-982556 A 20041104
WO 2004-US36784 W 20041105

AB The present invention provides methods for diagnosing mental disorders (e.g., psychotic disorders such as schizophrenia). The present invention uses DNA microarray anal. to demonstrate differential expression of genes in selected regions of post-mortem brains from patients diagnosed with mental disorders in comparison with normal control subjects. The invention also provides methods of identifying modulators of such mental disorders as well as methods of using these modulators to treat patients suffering from such mental disorders.

L4 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:248643 CAPLUS
DOCUMENT NUMBER: 142:274056
TITLE: Sequences of human schizophrenia related genes and use for diagnosis, prognosis and therapy
INVENTOR(S): Liew, Choong-Chin
PATENT ASSIGNEE(S): Chondrogene Limited, Can.
SOURCE: U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of U.S. Ser. No. 802,875.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 47
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004241727	A1	20041202	US 2004-812731	20040330
US 2004014059	A1	20040122	US 2002-268730	20021009
US 2005191637	A1	20050901	US 2004-803737	20040318
US 2005196762	A1	20050908	US 2004-803759	20040318
US 2005196763	A1	20050908	US 2004-803857	20040318
US 2005196764	A1	20050908	US 2004-803858	20040318
US 2005208505	A1	20050922	US 2004-803648	20040318
US 2004241727	A1	20041202	US 2004-812731	20040330

PRIORITY APPLN. INFO.: US 1999-115125P P 19990106
US 2000-477148 B1 20000104
US 2002-268730 A2 20021009
US 2003-601518 A2 20030620
US 2004-802875 A2 20040312
US 2004-812731 A 20040330

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing and monitoring diseases using gene-specific and/or tissue-specific primers. The present invention also describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstract record is one of 3 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L4 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:139371 CAPLUS
DOCUMENT NUMBER: 142:195820
TITLE: Gene expression profiles and biomarkers for the

detection of Chagas disease and other disease-related gene transcripts in blood
INVENTOR(S): Liew, Choong-Chin
PATENT ASSIGNEE(S): Chondrogene Limited, Can.
SOURCE: U.S. Pat. Appl. Publ., 154 pp., Cont.-in-part of U.S. Ser. No. 802,875.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 47
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004241729	A1	20041202	US 2004-813097	20040330
US 2004014059	A1	20040122	US 2002-268730	20021009
US 2005191637	A1	20050901	US 2004-803737	20040318
US 2005196762	A1	20050908	US 2004-803759	20040318
US 2005196763	A1	20050908	US 2004-803857	20040318
US 2005196764	A1	20050908	US 2004-803858	20040318
US 2005208505	A1	20050922	US 2004-803648	20040318
US 2004241729	A1	20041202	US 2004-813097	20040330

PRIORITY APPLN. INFO.:

US 1999-115125P	P	19990106
US 2000-477148	B1	20000104
US 2002-268730	A2	20021009
US 2003-601518	A2	20030620
US 2004-802875	A2	20040312
US 2004-813097	A	20040330

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing, and monitoring diseases, and in particular Chagas disease, using gene-specific and/or tissue-specific primers. Affymetrix Human Genome U133 and ChondroChip microarrays were used to detect differentially expressed gene transcripts in hypertension, obesity, allergy, systemic steroids, coronary artery disease, diabetes type 2, hyperlipidemia, lung disease, bladder cancer, rheumatoid arthritis, osteoarthritis, liver cancer, schizophrenia, Chagas disease, asthma, and manic depression syndrome. The present invention describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstract record is one of 3 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L4 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:308529 CAPLUS
DOCUMENT NUMBER: 140:333599
TITLE: Gene expression profile of human and mouse genes in atopic dermatitis and psoriasis patients and its use for diagnosis, therapy, and drug screening
INVENTOR(S): Itoh, Mikito; Ogawa, Kaoru; Shinagawa, Akira; Sudo, Hajime; Ogawa, Hideoki; Ra, Chisei; Mitsuishi, Kouichi
PATENT ASSIGNEE(S): Genox Research, Inc., Japan; Juntendo University
SOURCE: PCT Int. Appl., 611 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004031386	A1	20040415	WO 2003-JP9808	20030801
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003252326	A1	20040423	AU 2003-252326	20030801
PRIORITY APPLN. INFO.:			JP 2002-229318 A	20020806
			JP 2003-136543 A	20030514
			WO 2003-JP9808 W	20030801

AB This invention provides gene expression profile between a rash site and a no-rash site in a patient with atopic dermatitis or a patient with psoriasis. The invention also provides gene expression profile between a no-rash site in such a disease and a normal subject. Animal models, particularly mouse for those diseases are also claimed. The gene expression profile provided in this invention can be used for diagnosis, therapy, and drug screening for atopic dermatitis and psoriasis.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:220463 CAPLUS
DOCUMENT NUMBER: 140:265579
TITLE: High throughput directed evolution of proteins and peptides using two-dimensional rational mutagenesis scanning
INVENTOR(S): Gantier, Rene; Guyon, Thierry; Cruz Ramos, Hugo; Vega, Manuel; Drittanti, Lila
PATENT ASSIGNEE(S): Nautilus Biotech, Fr.
SOURCE: PCT Int. Appl., 431 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004022747	A1	20040318	WO 2003-IB4255	20030908
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2498284	A1	20040318	CA 2003-2498284	20030908
AU 2003267700	A1	20040329	AU 2003-267700	20030908
EP 1539950	A1	20050615	EP 2003-748392	20030908
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005202438	A1	20050915	US 2003-658355	20030908

US 2006020396	A1	20060126	US 2005-196067		20050802
PRIORITY APPLN. INFO.:			US 2002-410258P	P	20020909
			US 2003-457063P	P	20030321
			US 2002-409898P	P	20020909
			US 2003-457135P	P	20030321
			US 2003-658355	A1	20030908
			WO 2003-IB4255	W	20030908

AB The invention claims processes and systems for the high throughput directed evolution of peptides and proteins. It also provides a rational method for generating protein variants. The method relies on an indirect search for protein improvement for a particular activity, such as increased resistance to proteolysis, based on a rational amino acid replacement and sequence change at single or a limited number of amino acid positions at a time. The target amino acids are selected in silico for replacement and are referred to as "is-HIT target positions". The collection (or library) of all is-HITs represents the first dimension (target residue position) of the two-dimensional scanning methods. The second dimension is the replacing amino acids. The collection of mutant mols., or in silico candidate LEADS, is generated, tested and phenotypically characterized one-by-one, for example in addressable arrays. Optimized proteins having modified amino acid sequences at some regions along the protein that perform better than the starting sequence are identified and isolated. The methods were applied to interferonα -2b and interferon-β to obtain mutants with altered resistance to proteolysis and/or higher conformational stability.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:591215 CAPLUS
DOCUMENT NUMBER: 139:144956
TITLE: Ligand binding domains of cytokine which are linked via flexible polypeptide linker and uses in therapy
INVENTOR(S): Ross, Richard; Artymiuk, Peter; Sayers, Jon
PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003062276	A2	20030731	WO 2003-GB253	20030124
WO 2003062276	A3	20031016		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2510751	A1	20030731	CA 2003-2510751	20030124
EP 1468020	A2	20041020	EP 2003-702702	20030124
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005529583	T	20051006	JP 2003-562153	20030124

IN 2004KN00972	A	20060505	IN 2004-KN972		20040713
BR 2004003173	A	20060321	BR 2004-3173		20040730
US 2005214762	A1	20050929	US 2005-502344		20050511
US 2007054364	A1	20070308	US 2006-595991		20061113
PRIORITY APPLN. INFO.:			GB 2002-1679	A	20020125
			WO 2003-GB253	W	20030124
			US 2005-502344	B3	20050511

AB The invention relates to the provision of oligomeric polypeptides (dimers, trimers, etc) comprising the ligand binding domains of cytokines which are linked via flexible polypeptide linker mols. The linker mols. optionally comprise protease sensitive sites to modulate the release of biol. active cytokines when administered to a human or animal subject. The invention also relates to chemical crosslinkers wherein the chemical crosslinkers serve to link the ligand binding domains. The chimeric cytokine can be used for treating acromegaly, gigantism, GH deficiency, Turners syndrome, renal failure, osteoporosis, diabetes mellitus, cancer, obesity, insulin resistance, hyperlipidemia, hypertension, anemia, autoimmune and infectious disease, inflammatory disorders including rheumatoid arthritis.

L4 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2002:937303 CAPLUS
DOCUMENT NUMBER:	138:20443
TITLE:	Endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes
INVENTOR(S):	Kondo, Akihiro; Takeda, Takeshi; Mizutani, Shigetoshi; Tsujimoto, Yoshimasa; Takashima, Ryokichi; Enoki, Yuki; Kato, Ikunoshin
PATENT ASSIGNEE(S):	Takara Bio Inc., Japan
SOURCE:	Jpn. Kokai Tokkyo Koho, 386 pp. CODEN: JKXXAF
DOCUMENT TYPE:	Patent
LANGUAGE:	Japanese
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
JP 2002355079	A	20021210	JP 2002-69354		20020313
PRIORITY APPLN. INFO.:			JP 2001-73183	A	20010314
			JP 2001-74993	A	20010315
			JP 2001-102519	A	20010330

AB A method and kit for detecting endocrine-disrupting chems. using DNA microarrays are claimed. The method comprises preparing a nucleic acid sample containing mRNAs or cDNAs originating in cells, tissues, or organisms which have been brought into contact with a sample containing the endocrine disruptor. The nucleic acid sample is hybridized with DNA microarrays having genes affected by the endocrine disruptor or DNA fragments originating in these genes have been fixed. The results obtained are then compared with the results obtained with the control sample to select the gene affected by the endocrine disruptor. Genes whose expression is altered by tri-Bu tin, 4-octaphenol, 4-nonylphenol, di-N-Bu phthalate, dichlorohexyl phthalate, octachlorostyrene, benzophenone, diethylhexyl phthalate, diethylstilbestrol (DES), and 17-β estradiol (E2), were found in mice by DNA chip anal.

L4 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2002:353234 CAPLUS
DOCUMENT NUMBER:	136:359632
TITLE:	Long-acting cytokine derivatives and their pharmaceutical compositions
INVENTOR(S):	Shechter, Yoram; Fridkin, Matityahu; Goldwaser, Itzhak

PATENT ASSIGNEE(S): Yeda Research and Development Co., Ltd., Israel
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002036067	A2	20020510	WO 2001-IL1005	20011030
WO 2002036067	A3	20030109		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002014223	A5	20020515	AU 2002-14223	20011030
EP 1337270	A2	20030827	EP 2001-982682	20011030
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004131586	A1	20040708	US 2003-415668	20030902

PRIORITY APPLN. INFO.: IL 2000-139400 A 20001101
WO 2001-IL1005 W 20011030

AB Cytokine derivs. are provided bearing functional groups sensitive to mild basic conditions, such as fluorenylmethoxycarbonyl (Fmoc) and 2-sulfo-9-fluorenylmethoxycarbonyl (FMS), and pharmaceutical compns. comprising them. Preferred derivs. are those in which amino groups of the cytokine are substituted with FMS, for example FMS7-IFN-α2 and FMS3-IL-2. These cytokine derivs. can be administered as inactive or slightly active prodrugs and are capable of undergoing spontaneous regeneration into the parent bioactive drugs under in vivo physiol. conditions and in a homogeneous fashion. The cytokine prodrugs present higher metabolic stability and augmented bioavailability. For example, in an in vivo experiment designed for the evaluation of the anti-metastatic capacity of FMS3-IL-2, mice were inoculated i.v. on day (-3) with 105 D122 metastatic cells. Native IL-2 and FMS3-IL-2 were administered i.p. at high and moderate concns. (5000 ng and 500 ng, resp.) once daily for 30 days. Each group consists of 8 mice. The original protocol for anti-metastatic therapy implies identical dosages given twice a day. However, since prolongation of FMS3-IL-2 in serum is assumed, it is administered only once a day. Metastatic load in lungs of mice was weighed on day 30.

L4 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:795994 CAPLUS
DOCUMENT NUMBER: 132:31744
TITLE: Gene probes used for genetic profiling in healthcare screening and planning
INVENTOR(S): Roberts, Gareth Wyn
PATENT ASSIGNEE(S): Genostic Pharma Ltd., UK
SOURCE: PCT Int. Appl., 745 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964627	A2	19991216	WO 1999-GB1780	19990604

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:		
GB 1998-12099	A	19980606
GB 1998-13291	A	19980620
GB 1998-13611	A	19980624
GB 1998-13835	A	19980627
GB 1998-14110	A	19980701
GB 1998-14580	A	19980707
GB 1998-15438	A	19980716
GB 1998-15574	A	19980718
GB 1998-15576	A	19980718
GB 1998-16085	A	19980724
GB 1998-16086	A	19980724
GB 1998-16921	A	19980805
GB 1998-17097	A	19980807
GB 1998-17200	A	19980808
GB 1998-17632	A	19980814
GB 1998-17943	A	19980819

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the number of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide critical clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies which comprises of the identification of the core group of genes and their sequence variants required to provide a broad base of clin. prognostic information - "genostics". The "Genostic" profiling of patients and persons will radically enhance the ability of clinicians, healthcare professionals and other parties to plan and manage healthcare provision and the targeting of appropriate healthcare resources to those deemed most in need. The use of this invention could also lead to a host of new applications for such profiling technologies, such as identification of persons with particular work or environment related risk, selection of applicants for employment, training or specific opportunities or for the enhancing of the planning and organization of health services, education services and social services.

L4 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	1999:795993 CAPLUS
DOCUMENT NUMBER:	132:31743
TITLE:	Gene probes used for genetic profiling in healthcare screening and planning

INVENTOR(S): Roberts, Gareth Wyn
PATENT ASSIGNEE(S): Genostic Pharma Limited, UK
SOURCE: PCT Int. Appl., 149 pp.
CODEN: PIXXD
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964626	A2	19991216	WO 1999-GB1779	19990604
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2330929	A1	19991216	CA 1999-2330929	19990604
AU 9941586	A	19991230	AU 1999-41586	19990604
AU 766544	B2	20031016		
AU 9941587	A	19991230	AU 1999-41587	19990604
GB 2339200	A	20000119	GB 1999-12914	19990604
GB 2339200	B	20010912		
EP 1084273	A1	20010321	EP 1999-925207	19990604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2003528564	T	20030930	JP 2000-553616	19990604
US 2003198970	A1	20031023	US 2002-206568	20020729

PRIORITY APPLN. INFO.:		
GB 1998-12098	A	19980606
GB 1998-28289	A	19981223
GB 1998-16086	A	19980724
GB 1998-16921	A	19980805
GB 1998-17097	A	19980807
GB 1998-17200	A	19980808
GB 1998-17632	A	19980814
GB 1998-17943	A	19980819
US 1999-325123	B1	19990603
WO 1999-GB1779	W	19990604

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the number of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide critical clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies.

L4 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:360183 CAPLUS

DOCUMENT NUMBER: 131:183492
TITLE: Therapeutic intervention with complement and β-glucan in cancer
AUTHOR(S): Ross, Gordon D.; Vetvicka, Vaclav; Yan, Jun; Xia, Yu; Vetvickova, Jana
CORPORATE SOURCE: Department of Microbiology and Immunology, Department of Pathology, Division of Experimental Immunology and Immunopathology, University of Louisville, Louisville, KY, USA
SOURCE: Immunopharmacology (1999), 42(1-3), 61-74
CODEN: IMMUDP; ISSN: 0162-3109
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review and discussion with many refs. Complement (C) has two major effector systems available for host defense. The membrane attack complex (MAC) generated from components C5-C9 can form membrane-penetrating lesions that lead to cell death by causing a rapid loss of cytoplasmic components. The MAC is only effective against pathogens with outer phospholipid membranes, and cannot kill Gram-pos. bacteria or yeast whose membranes are protected by cell walls. The most important effector mechanism of C is the opsonization of microbial pathogens with the serum protein C3 that leads to their high avidity attachment to the C3-receptors of phagocytic cells. Pathogens that activate complement are first coated with the C3b fragment of C3, which is rapidly proteolyzed into the iC3b fragment by serum factor I. These iC3b fragments serve to promote the high avidity attachment of the 'iC3b-opsonized' pathogens to the iC3b-receptors (CR3, CD11b/CD18) of phagocytic cells and natural killer (NK) cells, stimulating phagocytosis and/or cytotoxic degranulation. Host cells, including neoplastic tumor cells, have been endowed with natural mechanisms for self-protection against both the MAC and the cytotoxic activation of CR3. This review discusses a novel type of immunotherapy for cancer that uses soluble yeast β-glucan to override the normal resistance of iC3b-opsonized tumor cells to the cytotoxic activation of phagocyte and NK cell CR3, allowing this important effector mechanism of the C system to function against tumor cells in the same way that it normally functions against bacteria and yeast. Moreover, the cytotoxic activation of β-glucan-primed NK cell CR3 by iC3b-opsonized tumors is shown to be accompanied by a tumor-localized secretion of the cytokines TNFα, IFNα, IFNγ, and IL-6.

REFERENCE COUNT: 116 THERE ARE 116 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:667965 CAPLUS
DOCUMENT NUMBER: 129:299458
TITLE: Cloning and cDNA sequences of human interferon α /β-binding proteins I and II and their pharmaceutical uses
INVENTOR(S): Novick, Daniela; Cohen, Batya; Rubinstein, Menachem
PATENT ASSIGNEE(S): Yeda Research and Development Co. Ltd., Israel
SOURCE: U.S., 35 pp., Cont.-in-part of U.S. Ser. No. 115,741, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 5821078	A	19981013	US 1995-385191		19950207
US 6458932	B1	20021001	US 1995-472402		19950607
JP 2004254695	A	20040916	JP 2004-90279		20040325
JP 2005162762	A	20050623	JP 2005-4934		20050112
JP 2005200422	A	20050728	JP 2005-33495		20050209
PRIORITY APPLN. INFO.:			IL 1992-103052	A	19920903
			IL 1993-106591	A	19930804
			US 1993-115741	B2	19930903
			IL 1994-108584	A	19940207
			JP 1993-243987	A3	19930902
			JP 1995-43539	A3	19950207
			US 1995-385191	A3	19950207

AB Interferon α /β binding proteins are provided, which are capable of modulating the activity of interferon-α subtypes as well as interferon-β. Cloning of DNA mols. encoding these proteins, expression in host cells and antibodies against the proteins are also provided. Type I interferons (IFN-α and IFN-β and IFN-ω) are a family of cytokines usually defined by their ability to confer resistance to viral infections. There are pathol. situations, related to these cytokines where neutralization of interferon activity may be beneficial to the patient. Cytokine-binding proteins (soluble cytokine receptors) correspond to the extracellular ligand binding domains of their resp. cell surface cytokine receptors. They are derived either by alternative splicing of pre-mRNA common to the cell surface receptor, or by proteolytic cleavage of the cell surface receptor. Therefore interferon α /β binding proteins were targeted that are capable of modulating the activity of interferon-. alpha. subtypes as well as interferon-β.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:91925 CAPLUS
DOCUMENT NUMBER: 124:139220
TITLE: Interferon-alpha/beta binding protein, its preparation and use
INVENTOR(S): Cohen, Batya; Novick, Daniela; Rubinstein, Menachem
PATENT ASSIGNEE(S): Israel
SOURCE: Can. Pat. Appl., 85 pp.
CODEN: CPXXEB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2141747	A1	19950808	CA 1995-2141747	19950203
AU 9511416	A	19950817	AU 1995-11416	19950127
AU 688430	B2	19980312		
FI 9500516	A	19950808	FI 1995-516	19950206
NO 9500420	A	19950808	NO 1995-420	19950206
NO 318912	B1	20050523		
EP 676413	A2	19951011	EP 1995-101560	19950206
EP 676413	A3	19960403		
EP 676413	B1	20050105		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
RU 2232811	C2	20040720	RU 1995-101848	19950206
AT 286509	T	20050115	AT 1995-101560	19950206
PT 676413	T	20050531	PT 1995-101560	19950206
ES 2236696	T3	20050716	ES 1995-101560	19950206

CN 1109505	A	19951004	CN 1995-100194		19950207
ZA 9500968	A	19951010	ZA 1995-968		19950207
JP 07298886	A	19951114	JP 1995-43539		19950207
JP 3670045	B2	20050713			
JP 2005200422	A	20050728	JP 2005-33495		20050209
PRIORITY APPLN. INFO.:			IL 1994-108584	A	19940207
			JP 1995-43539	A3	19950207

AB Type I interferons (IFN-α and IFN-β and IFN-ω) are a family of cytokines usually defined by their ability to confer resistance to viral infections. There are pathol. situations, related to these cytokines where neutralization of interferon activity may be beneficial to the patient. Cytokine binding proteins (soluble cytokine receptors) correspond to the extracellular ligand binding domains of their resp. cell surface cytokine receptors. They are derived either by alternative splicing of pre-mRNA common to the cell surface receptor, or by proteolytic cleavage of the cell surface receptor. Therefore interferon α /β binding proteins were targeted that are capable of modulating the activity of interferon-. alpha. subtypes as well as interferon-β. Cloning of DNA mols. encoding these proteins and expression in host cells and antibodies against these proteins is discussed.

L4 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	1995:332388 CAPLUS
DOCUMENT NUMBER:	122:104011
TITLE:	Resistance of recombinant proteins to proteolysis during folding and in the folded state
AUTHOR(S):	Fountoulakis, Michael
CORPORATE SOURCE:	Dep. of Biology, F. Hoffmann-La Roche Ltd., Basel, CH-4002, Switz.
SOURCE:	Journal of Chemical Technology & Biotechnology (1995), 62(1), 81-90 CODEN: JCTBED; ISSN: 0268-2575
PUBLISHER:	Wiley
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Protein purification often involves the use of denaturing agents for solubilization. During refolding, following removal of the denaturants, the proteins of interest are exposed to proteases present in the expression system. Here the resistance of selected recombinant proteins to three widely used proteolytic enzymes, trypsin (EC 3.4.21.4), proteinase K (EC 3.4.21.14) and endoproteinase Glu-C (EC 3.4.21.19), was investigated during folding and in the folded state. Target proteins and protease mixts. were denatured in 8 mol dm-3 urea and the proteins were allowed to refold by removal of the urea by dialysis. The proteolytic products were analyzed by sodium dodecyl sulfate-polyacrylamide gels and protein digestion during folding was compared with the digestion under similar conditions in physiol. buffer. Depending on the folding state of the proteins, the proteases had different effects on the substrates. During folding, certain recombinant proteins were more efficiently digested by trypsin and, in particular, by proteinase K in comparison with digestion in the folded state, while other protein substrates were more resistant to proteolytic degradation in a denatured or partially denatured state than their folded counterparts. Incubation of most substrate proteins with endoproteinase Glu-C yielded kinetics of digestion that were essentially similar for both partially folded and unfolded substrates. The results reported may be useful for protection of sensitive proteins and in studies of protein folding mechanisms.

L4 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1988:144742 CAPLUS
DOCUMENT NUMBER: 108:144742
TITLE: Identification and partial characterization of a novel protease in Saccharomyces cerevisiae which cleaves the peptide bond between residues 22 and 23 in α-interferon, and identification of an α-interferon resistant to said proteolysis
INVENTOR(S): O'Loughlin, John T.
PATENT ASSIGNEE(S): Interferon Sciences, Inc., USA
SOURCE: Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 240224	A2	19871007	EP 1987-302519	19870324
EP 240224	A3	19890201		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DK 8701614	A	19871001	DK 1987-1614	19870330
CN 87102497	A	19871111	CN 1987-102497	19870330
JP 62296892	A	19871224	JP 1987-74566	19870330

PRIORITY APPLN. INFO.: US 1986-845937 A 19860331

AB A novel S. cerevisiae protease cleaves α-interferons between basic amino acids at positions 22 and 23, but cleavage does not occur if residue 22 is serine. A recombinant interferon α with serine, threonine, asparagine, glutamine, or glycine at position 22 could be produced intact in a microorganism whose primary proteolytic activity against the natural species is at that site. The protease was partially purified. from a protease-deficient PEP 3-4 S. cerevisiae mutant. It was membrane-bound and activated by the Triton X-100 present during cell lysis. Recombinant interferons α -1, α-2, and α-8 were all incubated with the protease. Both α-2 and α-8 were cleaved between amino acids 22 and 23 (which were Arg-Lys and Arg-Arg, resp.), but α-1 (Ser-Arg) was not.

=> Log off H
SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 13:58:52 ON 25 MAR 2007

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAEGS1646

PASSWORD:
* * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE'
AT 14:18:26 ON 25 MAR 2007
FILE 'BIOSIS' ENTERED AT 14:18:26 ON 25 MAR 2007

FILE 'CAPLUS' ENTERED AT 14:18:26 ON 25 MAR 2007

FILE 'EMBASE' ENTERED AT 14:18:26 ON 25 MAR 2007

FILE 'MEDLINE' ENTERED AT 14:18:26 ON 25 MAR 2007

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	121.00	121.21
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-14.82	-14.82

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(FILE 'HOME' ENTERED AT 13:34:30 ON 25 MAR 2007)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE' ENTERED AT 13:34:48 ON 25 MAR 2007
L1 70256 S (INTERFERON ALPHA) OR IFN-ALPHA AND (MUTEIN OR VARIANT OR MUT
L2 248 S L1 AND PROTEOL?
L3 142 DUP REM L2 (106 DUPLICATES REMOVED)
L4 21 S L3 AND RESISTANCE

=> S L1 AND (IFN -alpha 2b)
L5 2141 L1 AND (IFN -ALPHA 2B)

=> S L5 AND Proteol?
L6 7 L5 AND PROTEOL?

=> Dup Rem l6
PROCESSING COMPLETED FOR L6
L7 3 DUP REM L6 (4 DUPLICATES REMOVED)

=> D ti L7 1-3

L7 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
TI High throughput directed evolution of proteins and peptides using two-dimensional rational mutagenesis scanning

L7 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1
TI Identification of a linear epitope of interferon-.alpha .2b recognized by neutralizing monoclonal antibodies

L7 ANSWER 3 OF 3 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 2
TI NATURAL HUMAN INTERFERON-ALPHA-2 IS O-GLYCOSYLATED.

=> D Ibib ABs L7 2,3

L7 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 1999:656689 CAPLUS
DOCUMENT NUMBER: 132:11491
TITLE: Identification of a linear epitope of interferon-α 2b recognized by neutralizing monoclonal antibodies
AUTHOR(S): Blank, Viviana C.; Sterin-Prync, Aida; Retegui, Lilia; Vidal, Alejandro; Criscuolo, Marcelo; Roguin, Leonor P.
CORPORATE SOURCE: Instituto de Quimica y Fisicoquimica Biologicas (UBA-CONICET), Facultad de Farmacia y Bioquimica, Buenos Aires, 1113, Argent.
SOURCE: European Journal of Biochemistry (1999), 265(1), 11-19
CODEN: EJBCAI; ISSN: 0014-2956

PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Four monoclonal antibodies (mAbs) directed against the recombinant human interferon-α 2b (IFN-α 2b) were used as probes to study the interaction of the IFN mol. to its receptors. The [125I]IFN-.alpha.2b binding to immobilized mAbs was completely inhibited by IFN-. alpha.2b and IFN-α2a but neither IFNβ nor IFNγ showed any effect. Gel-filtration HPLC of the immune complexes formed by incubating [125I]IFN-.alpha.2b with paired mAbs revealed the lack of simultaneous binding of two different antibodies to the tracer, suggesting that all mAbs recognize the same IFN antigenic domain. Furthermore, the mAbs were also able to neutralize the IFN-.alpha.2b anti-viral and anti-proliferative activities as well as [125I]IFN-. alpha.2b binding to WISH cell-membranes. As [125I]mAbs did not recognize IFN exposed epitopes in the IFN:receptor complexes, mAb induction of a conformational change in the IFN binding domain impairing its binding to receptors was considered unlikely. To identify the IFN region recognized by mAbs, IFN-.alpha.2b was digested with different proteolytic enzymes. Immunoreactivity of the resulting peptides was examined by Western blot and their sequences were established by Edman degradation after blotting to poly(vinylidene difluoride) membranes. Data obtained indicated that the smallest immunoreactive region recognized by mAbs consisted of residues 107-132 or 107-146. As this zone includes the sequence 123-140, which has been involved in the binding to receptors, and the authors' mAbs did not show an allosteric behavior, it is concluded that they are directed to overlapping epitopes located close to or even included in the IFN binding domain.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 3 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 2

ACCESSION NUMBER: 1991:360709 BIOSIS
DOCUMENT NUMBER: PREV199192048934; BA92:48934
TITLE: NATURAL HUMAN INTERFERON-ALPHA-2 IS O-GLYCOSYLATED.
AUTHOR(S): ADOLF G [Reprint author]; KALSNER I; AHORN H; MAURER-FOGY I; CANTELL K
CORPORATE SOURCE: ERNST-BOEHRINGER-INST, ARZNEIMITTELFORSCHUNG, BENDER AND CO BES MBH, DR BOEHRINGER-GASSE 5-11, A-1121 VIENNA, AUSTRIA
SOURCE: Biochemical Journal, (1991) Vol. 276, No. 2, pp. 511-518. ISSN: 0264-6021.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 13 Aug 1991
Last Updated on STN: 13 Aug 1991

AB Natural human interferon α 2 (IFN-α2) was isolated from a preparation of partially purified human leucocyte IFN by monoclonal-antibody immunoaffinity chromatography. The purified protein had a specific activity of 1.5 + 108 i.u./mg; it was estimated to constitute 10-20% of the total antiviral activity of leucocyte IFN. N-Terminal amino-acid-sequence analysis identified the subspecies IFN-.alpha.2b and/or IFN-α2c, whereas not detectable. The structure of natural IFN-α2 was found to differ from that of its recombinant (Escherichia coli-derived) equivalent. First, reverse-phase h.p.l.c. showed that natural IFN-α2 was signficiantly more hydrophilic than expected. Secondly, the apparent

molecular mass of the natural protein determined by SDS/PAGE was higher than that of recombinant IFN-α2; incubation under mild alkaline conditions known to eliminate O-linked carbohydrates resulted in a reduction of the apparent molecular mass to that of the recombinant protein. On sequence analysis of proteolytic peptides, Thr-106 was found to be modified. These results suggested that Thr-106 of natural IFN-α2 carries O-linked carbohydrates. Reverse-phase h.p.l.c. as well as SDS/PAGE of natural IFN-α2 showed that glycosylation is heterogeneous. For characterization of the carbohydrate moieties, the protein was treated with neuraminidase and/or O-glycanase and analysed by gel electrophoresis; in addition, glycopeptides obtained by proteinase digestion and separated by h.p.l.c. were characterized by sequence analysis and m.s. Further information on the composition of the glycans was obtained by monosaccharide analysis. The results indicate that natural IFN-α2 contains the disaccharide galactosyl-N-acetylgalactosamine (Gal-GalNAc) linked to the Thr-106. In part of the molecules, this core carbohydrate carries (α-)N-acetylneuraminic acid, whereas a disaccharide, probably N-acetyl-lactosamine, is bound to Gal-GalNAc in another proportion of the protein. Further glycosylation isomers are present in small amounts. As IFN-α2 is the only IFN-α species with a threonine residue at position 106, it may represent the only O-glycosylated human IFN-α protein.

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=> D Hist

     (FILE 'HOME' ENTERED AT 13:34:30 ON 25 MAR 2007)

     FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE' ENTERED AT 13:34:48 ON 25 MAR 2007
L1        70256 S (INTERFERON ALPHA) OR IFN-ALPHA AND (MUTEIN OR VARIANT OR MUT
L2          248 S L1 AND PROTEOL?
L3          142 DUP REM L2 (106 DUPLICATES REMOVED)
L4           21 S L3 AND RESISTANCE
L5         2141 S L1 AND (IFN -ALPHA 2B)
L6            7 S L5 AND PROTEOL?
L7            3 DUP REM L6 (4 DUPLICATES REMOVED)

=> S L5 AND glycosyl?
L8           21 L5 AND GLYCOSYL?

=> Dup Rem L8
PROCESSING COMPLETED FOR L8
L9           12 DUP REM L8 (9 DUPLICATES REMOVED)

=> D Ti L9 1-12

L9   ANSWER 1 OF 12  CAPLUS  COPYRIGHT 2007 ACS on STN DUPLICATE 1
TI   Treatment of interferon-α  for chronic hepatitis
     C

L9   ANSWER 2 OF 12  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
     DUPLICATE 2
TI   GlycoPEGylation of recombinant therapeutic proteins produced in
     Escherichia coli.

L9   ANSWER 3 OF 12  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Study on mechanism of interferon treating pathological scars

L9   ANSWER 4 OF 12  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   High throughput directed evolution of proteins and peptides using
     two-dimensional rational mutagenesis scanning
```

L9 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
TI Methods and compositions relating to isoleucine boroproline compounds

L9 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
TI Providing natural allelic variants of interferon .alpha
. as therapeutic agents with high therapeutic index

L9 ANSWER 7 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI In vitro O-glycosylation of E. coli-produced therapeutic
proteins using recombinant glycosyltransferases.

L9 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 3
TI Structural characterization of N-linked and O-linked oligosaccharides
derived from interferon-α 2b and
interferon-α 14c produced by Sendai-virus-induced
human peripheral blood leukocytes

L9 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 4
TI Identification of nine interferon-α subtypes
produced by Sendai virus-induced human peripheral blood leukocytes

L9 ANSWER 10 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
TI Carbohydrate composition of natural source human-leukocyte derived
interferon-alphan3.

L9 ANSWER 11 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 5
TI Expression and purification of recombinant, glycosylated human
interferon alpha 2b in murine myeloma NSo cells.

L9 ANSWER 12 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 6
TI NATURAL HUMAN INTERFERON-ALPHA-2 IS O-
GLYCOSYLATED.

=> D Ibib ABS L9 1-3, 5-11

L9 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2006:507346 CAPLUS
DOCUMENT NUMBER: 145:416104
TITLE: Treatment of interferon-α
for chronic hepatitis C
AUTHOR(S): Moriyama, Mitsuhiko; Arakawa, Yasuyuki
CORPORATE SOURCE: Division of Gastroenterology and Hepatology,
Department of Medicine, Nihon University School of
Medicine, Itabashi-ku, Tokyo, 173-8610, Japan
SOURCE: Expert Opinion on Pharmacotherapy (2006), 7(9),
1163-1179
CODEN: EOPHF7; ISSN: 1465-6566
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Combination therapy with polyethylene glycosylated
IFN-α2a or IFN-.alpha.2b and ribavirin
is currently the standard therapy for chronic hepatitis C. However, even with
this therapy, hepatitis C virus cannot be eradicated in 50% of patients
with refractory chronic hepatitis C. In addition, withdrawal or dose reduction
occurs in .apprx. 40% of patients due to adverse effects. This treatment
is also a contraindication in some patients, such as in patients with
coexisting diseases or in elderly patients. For these patients, standard

IFN-α monotherapy is even safer and more effective. In patients with chronic hepatitis C, IFN-α monotherapy results in a significant increase in the cumulative survival rate by suppressing the progression to hepatocellular carcinoma or liver failure. In addition, other efficacious therapeutic regimens have been employed, such as prolonged administration of standard IFN-α in elderly patients; prolonged low-dose continuous administration in patients with decompensated cirrhosis or hepatocellular carcinoma postoperative patients; and combination therapy with 5-fluorouracil and standard IFN-α for advanced hepatocellular carcinoma. Monotherapy with standard IFN-α should thus be recognized as one of the important therapeutic strategies for chronic hepatitis C.

REFERENCE COUNT: 84 THERE ARE 84 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 2

ACCESSION NUMBER: 2006:544386 BIOSIS
DOCUMENT NUMBER: PREV200600541473
TITLE: GlycoPEGylation of recombinant therapeutic proteins produced in Escherichia coli.
AUTHOR(S): DeFrees, Shawn; Wang, Zhi-Guang; Xing, Ruye; Scott, Arthur E.; Wang, Jin; Zopf, David [Reprint Author]; Gouty, Dominique L.; Sjoberg, Eric R.; Panneerselvam, Krishnasamy; Brinkman-Van der Linden, Els C. M.; Bayer, Robert J.; Tarp, Mads A.; Clausen, Henrik
CORPORATE SOURCE: Neose Technol Inc, 102 Witmer Rd Dr, Horsham, PA 19044 USA dzopf@neose.com
SOURCE: Glycobiology, (SEP 2006) Vol. 16, No. 9, pp. 833-843. ISSN: 0959-6658.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 18 Oct 2006
Last Updated on STN: 18 Oct 2006

AB Covalent attachment of polyethylene glycol, PEGylation, has been shown to prolong the half-life and enhance the pharmacodynamics of therapeutic proteins. Current methods for PEGylation, which rely on chemical conjugation through reactive groups on amino acids, often generate isoforms in which PEG is attached at sites that interfere with bioactivity. Here, we present a novel strategy for site-directed PEGylation using glycosyltransferases to attach PEG to O-glycans. The process involves enzymatic GalNAc glycosylation at specific serine and threonine residues in proteins expressed without glycosylation in Escherichia coli, followed by enzymatic transfer of sialic acid conjugated with PEG to the introduced GatNAc residues. The strategy was applied to three therapeutic polypeptides, granulocyte colony stimulating factor (G-CSF), interferon-alpha2b (IFN-alpha 2b), and granulocyte/macrophage colony stimulating factor (GM-CSF), which are currently in clinical use.

L9 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:714620 CAPLUS
DOCUMENT NUMBER: 146:272215
TITLE: Study on mechanism of interferon treating pathological scars
AUTHOR(S): Lu, Xin-an; Xu, Ming; Shen, Guo-liang; Lin, Wei; Zhao, Xiao-yu
CORPORATE SOURCE: Dept of Burn and Plastic Surgery, The First Hospital Affiliated to Suzhou University, Jiangsu Suzhou, 215006, Peop. Rep. China
SOURCE: Suzhou Daxue Xuebao, Yixueban (2005), 25(6), 1091-1093, 1103
CODEN: SDXYC2; ISSN: 1673-0399

PUBLISHER: Suzhou Daxue Chubanshe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB This paper studied the effect of interferon (IFN) on transforming growth factor-β1 (TGF-β1), matrix metalloprotease-1 (MMP-1), platelet-derived growth factor-BB (PDGF-BB), and glycosyltransferase (ppGalNAc-T2) in fibroblasts of pathol. scars and the mechanism of interferon on pathol. scars. The fibroblasts of pathol. scars were cultured by the method of tissue culture and were randomized in 3 groups: control (0.9% sodium chloride), low concentration (100 u/mL IFN α -2b), and high concentration (10000 u/mL IFN α -2b). The expression of TGF-β1, MMP-1, PDGF-BB, and ppGalNAc-T2 were analyzed by RT-PCR in each group. The results showed that after treating cultured fibroblasts of pathol. scars with 100 u/mL IFN α -2b and 10000 u/mL IFN α -2b, the expression of TGF-β1, PDGF-BB, and ppGalNAc-T2 mRNA were lower than that in the control group, and the expression of MMP-1 mRNA was higher than that of control group. The result was significantly different and was related with the concentration in the IFN α -2b. In conclusion, the cause of good effect of IFN . alpha.-2b on inhibiting fibroblast of pathol. scars may relate with some kinds of cellular factors, such as TGF-β1 and PDGF-BB.

L9 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:41226 CAPLUS
DOCUMENT NUMBER: 140:105321
TITLE: Methods and compositions relating to isoleucine boroproline compounds
INVENTOR(S): Adams, Sharlene; Miller, Glenn T.; Jesson, Michael I.; Jones, Barry
PATENT ASSIGNEE(S): Point Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004004658	A2	20040115	WO 2003-US21405	20030709
WO 2004004658	A3	20050804		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2491466	A1	20040115	CA 2003-2491466	20030709
AU 2003265264	A1	20040123	AU 2003-265264	20030709
US 2004077601	A1	20040422	US 2003-616694	20030709
US 2005084490	A1	20050421	US 2003-616409	20030709
EP 1578434	A2	20050928	EP 2003-763380	20030709
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006507352	T	20060302	JP 2004-562634	20030709

CN 1802090	A	20060712	CN 2003-821282		20030709
CN 1826129	A	20060830	CN 2003-821281		20030709
IN 2005KN00151	A	20050916	IN 2005-KN151		20050208
PRIORITY APPLN. INFO.:			US 2002-394856P	P	20020709
			US 2002-414978P	P	20021001
			US 2003-466435P	P	20030428
			WO 2003-US21405	W	20030709

OTHER SOURCE(S): MARPAT 140:105321

AB A method for treating subjects with, inter alia, abnormal cell proliferation or infectious disease using agents of formula (I, AmNHCH(CH(CH3)CH2CH3)COA1R) (where Am and A1 are amino acids and R = organo boronates, organo phosphonates, fluoroalkyl ketones, alphaketos, N-peptidyl-O-(acylhydroxylamines), azapeptides, azetidines, fluoroolefins dipeptide isosteres, peptidyl (α-aminoalkyl) phosphonate esters, aminoacyl pyrrolidine-2-nitriles and 4-cyanothiazolidides) is claimed. Methods for stimulating an immune response using the compds. of the invention are also claimed. Compns. containing Ile-boroPro compds. are also provided as are kits containing the compns. The invention embraces the use of these compds. alone or in combination with other therapeutic agents.

L9 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:39591 CAPLUS

DOCUMENT NUMBER: 140:92604

TITLE: Providing natural allelic variants of interferon α as therapeutic agents with high therapeutic index

INVENTOR(S): Escary, Jean-Louis

PATENT ASSIGNEE(S): Fr.

SOURCE: U.S. Pat. Appl. Publ., 16 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004009161	A1	20040115	US 2002-315493	20021210
EP 1418428	A1	20040512	EP 2002-292787	20021107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
CA 2413981	A1	20040507	CA 2002-2413981	20021211
CA 2504980	A1	20040521	CA 2003-2504980	20031106
WO 2004042394	A2	20040521	WO 2003-EP13695	20031106
WO 2004042394	A3	20040715		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003294782	A1	20040607	AU 2003-294782	20031106
EP 1561105	A2	20050810	EP 2003-785733	20031106
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2006094641	A1	20060504	US 2005-534098	20050506
PRIORITY APPLN. INFO.:			EP 2002-292787 A	20021107
			US 2002-315493 A	20021210

AB Disclosed are methods for identifying and providing new therapeutic agent(s) by selecting at least one polypeptide encoded by a natural allelic variant of one preselected gene having a therapeutic potential and determining the therapeutic index of the selected polypeptide(s) and retaining as therapeutic agent(s) those polypeptide(s) whose therapeutic index is higher than that of a reference agent. The invention is illustrated by tests performed on the polypeptides encoded by natural allelic variants of 3 genes belonging to the interferon α gene family and representing: C122S IFNα-5; G45R IFNα-17; and Q114H/V127D IFNα-21 and K179E IFNα-21. The polypeptides encoded by the natural allelic variants of IFNα are subjected to several activity tests to determine their therapeutic suitability and are also compared with the product on the market, IFNα -2b (Intron A). The antiproliferative activities of the above variants were performed in tests on human lymphoblasts (Daudi cells) and their antiviral activities were evaluated in both virus-infected cell cultures (human WISH cells infection with vascular stomatitis virus) and mouse models (encephalomyocarditis virus and Friend erythroleukemia virus) of viral infection. The immunomodulatory activities of the above variants were tested on human dendritic cell maturation and a safety pharmacol. study was performed in conscious Rhesus monkeys.

L9 ANSWER 7 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:321840 BIOSIS
DOCUMENT NUMBER: PREV200510111622
TITLE: In vitro O-glycosylation of E. coli-produced therapeutic proteins using recombinant glycosyltransferases.
AUTHOR(S): Defrees, Shawn [Reprint Author]; Wang, Zhi-Guang; Scott, Arthur E.; Wang, Jin; Xing, Ruye; Zopf, David; Gouty, Dominique L.; Sjoberg, Eric R.; Panneerselvam, Krishnasamy; Brinkman-Van der Linden, Els C. M.; Bayer, Robert J.; Tarp, Mads A.; Clausen, Henrik
CORPORATE SOURCE: Neose Technol Inc, Horsham, PA USA
SOURCE: Glycobiology, (NOV 2004) Vol. 14, No. 11, pp. 1086. Meeting Info.: Joint Meeting of the Society-for-Glycobiology/Japanese-Society-for-Carbohydrate-Research. Honolulu, HI, USA. November 17 -20, 2004. Soc Gylcobiol; Japanese Soc Carbohydrate Res. ISSN: 0959-6658.
DOCUMENT TYPE: Conference; (Meeting) Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Aug 2005 Last Updated on STN: 25 Aug 2005

L9 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 1998:266317 CAPLUS
DOCUMENT NUMBER: 129:39864
TITLE: Structural characterization of N-linked and O-linked oligosaccharides derived from interferon-. alpha.2b and interferon-. alpha.14c produced by Sendai-virus-induced human peripheral blood leukocytes
AUTHOR(S): Nyman, Tuula A.; Kalkkinen, Nisse; Tolo, Hannele; Helin, Jari
CORPORATE SOURCE: Institute of Biotechnology, Protein Chemistry Lab., University of Helsinki, Finland
SOURCE: European Journal of Biochemistry (1998), 253(2), 485-493 CODEN: EJBCAI; ISSN: 0014-2956

PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors have previously isolated and partially characterized the components of a highly purified interferon-α (IFN-α) preparation produced by Sendai-virus-induced human peripheral blood leukocytes. Nine IFN-α species were identified, and two of these were glycosylated. Here, the authors isolated the N-linked oligosaccharides of IFN-α14c and the O-linked chains of IFN-.alpha.2b, and the glycans were characterized by electrospray tandem mass spectrometry and by specific glycosidase digestions monitored by matrix-assisted laser desorption ionization time of flight mass spectrometry. The IFN-α14c N-glycans were shown to exhibit core-fucosylated biantennary glycans, with about 10% carrying an addn1. α1,3-linked fucose unit at the antennae. The IFN-.alpha.2b was shown to carry about 50% core type-1 disialytetrasaccharides, 30% core type-1 monosialyltrisaccharides and 20% core type-2 monosialylpentasaccharides.
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 1998:70613 CAPLUS
DOCUMENT NUMBER: 128:179185
TITLE: Identification of nine interferon-. alpha. subtypes produced by Sendai virus-induced human peripheral blood leukocytes
AUTHOR(S): Nyman, Tuula A.; Tolo, Hannele; Parkkinen, Jaakko; Kalkkinen, Nisse
CORPORATE SOURCE: Institute of Biotechnology, Protein Chemistry Laboratory, University of Helsinki, FIN-00014, Finland
SOURCE: Biochemical Journal (1998), 329(2), 295-302
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The human interferon-α (IFN-. alpha.) family is encoded by 13 different functional genes, and including all cloned sequence variants there are 28 potential IFN-α proteins. To find out which of the described sequences are expressed in normal human leukocytes, we have isolated and partly characterized the components of a highly purified IFN-α preparation produced by Sendai virus-induced human peripheral blood leukocytes. The identification protocol consisted of N-terminal sequencing and mass mapping of the proteins separated by reverse-phase HPLC and/or SDS/-PAGE. The highly purified leukocyte IFN-α preparation was found to contain at least nine different IFN-α species: IFN-. alpha.1a, IFN-.alpha.2b, IFN -α 4b, IFN-α 7a, IFN-. alpha.8b, IFN-α 10a, IFN-. alpha.14c, IFN-α 17b, and IFN-. alpha.21b. IFN-α 1a was the major subtype, comprising approx. 30% of total leukocyte IFN-. alpha.. IFN-α 14c, the only subtype containing potential N-glycosylation sites, was shown to be glycosylated at Asn-72. Mol. mass determination of the intact proteins by electrospray ionization MS showed that there are no other post-translational modifications in the IFN-α subtypes than the glycosylation of IFN-.alpha .2b and IFN-α 14c. Only one sequence variant was found for each subtype, suggesting that the other

described gene sequences represent allelic variants or mutations that are more rarely found in the general population.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 10 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1998:58374 BIOSIS
DOCUMENT NUMBER: PREV199800058374
TITLE: Carbohydrate composition of natural source human-leukocyte derived interferon-alphan3.
AUTHOR(S): Lawrynowicz, Witold J.; Lin, Xi; Lee, Shu-Ying; Ferencz-Biro, Katalin; Liao, Mei-June
CORPORATE SOURCE: Interferon Sci. Inc., New Brunswick, NJ 08901, USA
SOURCE: Journal of Interferon and Cytokine Research, (Oct., 1997) Vol. 17, No. SUPPL. 2, pp. S106. print.
Meeting Info.: Annual Meeting of the International Society for Interferon and Cytokine Research. San Diego, California, USA. October 19-24, 1997. International Society for Interferon and Cytokine Research.
ISSN: 1079-9907.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Jan 1998
Last Updated on STN: 30 Jan 1998

L9 ANSWER 11 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 5
ACCESSION NUMBER: 1996:331039 BIOSIS
DOCUMENT NUMBER: PREV199699053395
TITLE: Expression and purification of recombinant, glycosylated human interferon alpha 2b in murine myeloma NSo cells.
AUTHOR(S): Rossmann, Cornelia; Sharp, Nigel; Allen, Geoffrey; Gewert, Dirk [Reprint author]
CORPORATE SOURCE: Cell Mol. Biol., Astra Draco AB, P.O. Box 34, S221 00 Lund, Sweden
SOURCE: Protein Expression and Purification, (1996) Vol. 7, No. 4, pp. 335-342.
CODEN: PEXPEJ. ISSN: 1046-5928.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Jul 1996
Last Updated on STN: 27 Jul 1996
AB We have expressed recombinant human interferon-alpha -2b in mammalian cells and isolated cell lines constitutively secreting very high levels of biologically active protein. The expression system takes advantage of the strong human cytomegalovirus immediate early promoter in mouse myeloma NSo cells and glutamine synthetase as a selectable marker; spontaneous mutants with amplified gene copy numbers were selected by growth of primary transfectants in the presence of methionine sulfoximine. Using this procedure, we have isolated a recombinant NSo cell line which secretes human interferon at the rate of 20 mu-g/10-6 cells/24 h and accumulates up to 120 mu-g/ml (apprx 2.4 times 10-7 U/ml) following prolonged undiluted culture. The interferon (IFN) could be efficiently purified on a polyclonal bovine anti-human IFN-alpha specific antibody column and the glycosylation pattern was found to be similar to that of nonrecombinant IFN-alpha-2b purified from virus-induced human Namalwa cells. The biological activity of the

recombinant material was indistinguishable from that of natural IFN from Namalwa cells, and the specific antiviral activity, as assayed on human HeLa cells challenged with encephalomyocarditis virus, was 2 times 10-8 IU/mg, similar to that of nonrecombinant IFN preparations. This represents the highest reported level of glycosylated, recombinant IFN expression in a stable mammalian system and is a significant advance in the large-scale production of these clinically important cytokines.

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PASSWORD:
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AT 14:41:14 ON 25 MAR 2007
FILE 'BIOSIS' ENTERED AT 14:41:14 ON 25 MAR 2007
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FILE 'CAPLUS' ENTERED AT 14:41:14 ON 25 MAR 2007
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-20.28	-20.28

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(FILE 'HOME' ENTERED AT 13:34:30 ON 25 MAR 2007)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE' ENTERED AT 13:34:48 ON 25 MAR 2007
L1 70256 S (INTERFERON ALPHA) OR IFN-ALPHA AND (MUTEIN OR VARIANT OR MUT
L2 248 S L1 AND PROTEOL?
L3 142 DUP REM L2 (106 DUPLICATES REMOVED)
L4 21 S L3 AND RESISTANCE
L5 2141 S L1 AND (IFN -ALPHA 2B)
L6 7 S L5 AND PROTEOL?
L7 3 DUP REM L6 (4 DUPLICATES REMOVED)
L8 21 S L5 AND GLYCOSYL?
L9 12 DUP REM L8 (9 DUPLICATES REMOVED)

=> S L1 AND ((Increased Activity)(S)antiviral)
L10 0 L1 AND ((INCREASED ACTIVITY)(S) ANTIVIRAL)

=> S L1 AND ((Increased Activity)(S)anti-proliferative)

```
L11          0 L1 AND ((INCREASED ACTIVITY)(S) ANTI-PROLIFERATIVE)

=> S L1 AND  (Activity)(S)antiviral)
UNMATCHED RIGHT PARENTHESIS 'ANTIVIRAL)'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> S L1 AND  (Activity(S)antiviral)
L12       3560 L1 AND (ACTIVITY(S) ANTIVIRAL)

=> S L1 AND (Activity(S)anti-proliferative)
L13         93 L1 AND (ACTIVITY(S) ANTI-PROLIFERATIVE)

=> Dup Rem L12
PROCESSING IS APPROXIMATELY  56% COMPLETE FOR L12
PROCESSING COMPLETED FOR L12
L14        2040 DUP REM L12 (1520 DUPLICATES REMOVED)

=> S L14 AND ((IFN-alpha 2b) OR IFNalpha-2b)
L15         71 L14 AND ((IFN-ALPHA 2B) OR IFNALPHA-2B)

=> S L13 AND ((IFN-alpha 2b) OR IFNalpha-2b)
L16          3 L13 AND ((IFN-ALPHA 2B) OR IFNALPHA-2B)

=> Dup Rem L16
PROCESSING COMPLETED FOR L16
L17           2 DUP REM L16 (1 DUPLICATE REMOVED)

=> D Ti L17 1-2

L17  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2007 ACS on STN  DUPLICATE 1
TI   Identification of a linear epitope of interferon-.alpha
     .2b recognized by neutralizing monoclonal antibodies

L17  ANSWER 2 OF 2  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
TI   Natural killer cell activity against cultured melanoma cells: A
     dye-reduction technique with studies on augmented activity by interferon
     subtypes.


=> D Ibib L17 2

L17  ANSWER 2 OF 2  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
ACCESSION NUMBER:   1993:30348  BIOSIS
DOCUMENT NUMBER:    PREV199395018548
TITLE:              Natural killer cell activity against cultured melanoma
                    cells: A dye-reduction technique with studies on augmented
                    activity by interferon subtypes.
AUTHOR(S):          Losinno, Carmela; Wines, Bruce D.; Mackay, Terrance G.
                    Johns And Ian R. [Reprint author]
CORPORATE SOURCE:   Cent. Mol. Biol. Med., Monash Univ., Clayton, Victoria
                    3168, Australia
SOURCE:             Natural Immunity, (1992) Vol. 11, No. 4, pp. 215-224.
                    ISSN: 1018-8916.
DOCUMENT TYPE:      Article
LANGUAGE:           English
ENTRY DATE:         Entered STN: 23 Dec 1992
                    Last Updated on STN: 24 Dec 1992


=> S L14 AND Proteol?
L18          15 L14 AND PROTEOL?
```

=> D Ti L18 1-15

L18 ANSWER 1 OF 15 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Induction of APOBEC3 family proteins, a defensive maneuver underlying interferon-induced anti-HIV-1 activity.

L18 ANSWER 2 OF 15 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI TGF-beta 1 mRNA expression in liver biopsy specimens and TGF-beta 1 serum levels in patients with chronic hepatitis C before and after antiviral therapy.

L18 ANSWER 3 OF 15 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Prolonging the half-life of human interferon-alpha2 in circulation: Design, preparation, and analysis of (2-sulfo-9-fluorenylmethoxycarbonyl)7-interferon-alpha2.

L18 ANSWER 4 OF 15 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Hybrid (BDBB) interferon-alpha: Preformulation studies.

L18 ANSWER 5 OF 15 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI NATURAL HUMAN INTERFERON-ALPHA-2 IS O-GLYCOSYLATED.

L18 ANSWER 6 OF 15 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI BIOLOGIC ACTIVITY IN A FRAGMENT OF RECOMBINANT HUMAN INTERFERON ALPHA.

L18 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
TI High throughput directed evolution of proteins and peptides using two-dimensional rational mutagenesis scanning

L18 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
TI Proteolytic degradation of the recombinant target protein, interferon-τ during its fermentative production in the methylotrophic yeast, Pichia pastoris

L18 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
TI The Nonstructural NS5A Protein of Hepatitis C Virus: An Expanding, Multifunctional Role in Enhancing Hepatitis C Virus Pathogenesis

L18 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
TI Long-acting cytokine derivatives and their pharmaceutical compositions

L18 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
TI Identification of a linear epitope of interferon-.alpha .2b recognized by neutralizing monoclonal antibodies

L18 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
TI Structural organization of the interferon molecules as precursors of immuno- and neuroactive oligopeptides

L18 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
TI Modified (1-28) beta interferons

L18 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
TI A new mass-spectrometric C-terminal sequencing technique finds a similarity between γ-interferon and α2-interferon and identifies a proteolytically clipped γ-interferon that retains full antiviral activity

L18 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

TI Interferon-mediated inhibition of production of Gazdar murine sarcoma virus, a retrovirus lacking env proteins and containing an uncleaved gag precursor

=> D Ibib Abs L18 3, 4, 13, 14

L18 ANSWER 3 OF 15 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:147461 BIOSIS
DOCUMENT NUMBER: PREV200100147461
TITLE: Prolonging the half-life of human interferon-alpha2 in circulation: Design, preparation, and analysis of (2-sulfo-9-fluorenylmethoxycarbonyl)7-interferon-alpha2.
AUTHOR(S): Shechter, Yoram [Reprint author]; Preciado-Patt, Liana; Schreiber, Gideon; Fridkin, Mati
CORPORATE SOURCE: Department of Biological Chemistry, Weizmann Institute of Science, Rehovot, 76100, Israel
yoram.shechter@weizmann.ac.il; mati.fridkin@weizmann.ac.il
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (January 30, 2001) Vol. 98, No. 3, pp. 1212-1217. print.
CODEN: PNASA6. ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Mar 2001
Last Updated on STN: 15 Feb 2002
AB Polypeptide drugs are generally short-lived species in circulation. In this study, we have covalently linked seven moieties of 2-sulfo-9-fluorenylmethoxycarbonyl (FMS) to the amino groups of human interferon-alpha2. The derivative thus obtained (FMS7-IFN-alpha2) has apprxeq4% the biological potency and 33 +- 4% the receptor binding capacity of the native cytokine. Upon incubation, FMS7-IFN-alpha2 undergoes time-dependent spontaneous hydrolysis, generating active interferon with t1/2 values of 24 +- 2 h at pH 8.5 and 98 +- 10 h at pH 7.4. When native IFN- alpha2 is intravenously administered to mice, circulating antiviral activity is maintained for a short duration and then declines with t1/2 = 4 +- 0.5 h, reaching undetectable values at apprxeq18 h after administration. With intravenously administered FMS7-IFN-alpha2, there is a lag period of 2 h, followed by a progressive elevation in circulating antiviral-active protein, which peaked at 20 h and declined with t1/2 = 35 +- 4 h. FMS7-IFN-alpha2 is resistant to alpha-chymotrypsin digest and to proteolytic inactivation by human serum proteases in vitro. We have thus introduced here an inactive IFN-alpha2 derivative, which is resistant to in situ inactivation and has the capability of slowly reverting to the native active protein at physiological conditions in vivo and in vitro. Having these attributes, FMS7-IFN-alpha2 maintains prolonged circulating antiviral activity in mice, exceeding 7-8 times the activity of intravenously administered native cytokine.

L18 ANSWER 4 OF 15 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1999:521402 BIOSIS
DOCUMENT NUMBER: PREV199900521402
TITLE: Hybrid (BDBB) interferon-alpha: Preformulation studies.
AUTHOR(S): Allen, John D.; Bentley, David; Stringer, Rowan A.; Lowther, Nicholas [Reprint author]
CORPORATE SOURCE: Drug Preformulation and Delivery Department, Ciba Pharmaceuticals (now Novartis Horsham Research Centre), Wimblehurst Road, Horsham, West Sussex, RH12 5AB, UK
SOURCE: International Journal of Pharmaceutics (Amsterdam), (Oct.

5, 1999) Vol. 187, No. 2, pp. 259-272. print.
CODEN: IJPHDE. ISSN: 0378-5173.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Dec 1999
Last Updated on STN: 3 Dec 1999

AB A number of techniques, including RP-HPLC, HP-SEC and SDS-PAGE have been used in the delineation of degradative mechanisms of recombinant hybrid (BDBB) interferon-alpha (IFN-alpha) in the solution phase. Different degradation profiles are found according to medium pH. At pH 4.0 the major routes of degradation are via chemical transformation of the monomeric protein to a species which retains antiviral activity, and by self-proteolytic hydrolysis. At pH 7.6, methionine-oxidation is the major chemical degradative process. Protein aggregation is also a significant route of degradation at the higher pH. The results have assisted in a targeted preformulation screen of potentially stabilising excipients and possible parenteral solution dosage forms have been identified. Preliminary 'real-time' storage data confirm excellent chemical and physical stability of IFN-alpha in vehicles formulated at pH 7.6 or, especially, pH 4.0 under the proposed shelf conditions.

L18 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1985:417791 CAPLUS
DOCUMENT NUMBER: 103:17791
TITLE: Modified (1-28) beta interferons
INVENTOR(S): Bell, Leslie D.; Boseley, Paul G.; Smith, John C.; Houghton, Michael
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: Eur. Pat. Appl., 64 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 130566	A1	19850109	EP 1984-107458	19840628
EP 130566	B1	19871028		
R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
US 4738844	A	19880419	US 1984-623814	19840622
US 4753795	A	19880628	US 1984-623601	19840622
US 4793995	A	19881227	US 1984-623815	19840622
US 4738845	A	19880419	US 1984-623894	19840625
AU 8429981	A	19850103	AU 1984-29981	19840628
AU 577789	B2	19881006		
AU 8429982	A	19850103	AU 1984-29982	19840628
AU 577790	B2	19881006		
AU 8429983	A	19850103	AU 1984-29983	19840628
AU 577791	B2	19881006		
AU 8429984	A	19850103	AU 1984-29984	19840628
AU 577792	B2	19881006		
JP 60100599	A	19850604	JP 1984-137079	19840702
JP 60105700	A	19850611	JP 1984-137081	19840702
JP 60143000	A	19850729	JP 1984-137080	19840702
JP 60214800	A	19851028	JP 1984-137078	19840702

PRIORITY APPLN. INFO.: GB 1983-17880 A 19830701

AB Recombinant DNA mols. are constructed which encode modified human β-interferon (IFN-β) mols. The modification involves replacement by 3-28 amino acids of amino acids nos. 1-28, in some cases by amino acids 2-28 from α-interferon. Plasmid vectors for these

modified IFN mols. are also prepared One modified IFN-β contains serine at position 16 in place of cysteine. Other IFNs contain α-IFN sequences. These modified interferons (designated group I IFNs) display some of the following properties; greater antiproliferative or antiviral activity, modified affinity for cell surface receptors, increased therapeutic index, increased stability in proteolysis, increased solubility in vivo, and greater ease of purification or recovery from bacterial exts. Pharmaceutical compns. containing these modified mols. are used to treat viral infections, regulate cell growth (as an antineoplastic agent), or regulate the immune system. Thus, amino acids 1-28 were replaced in groups of 3-28 amino acids by the insertion of chemical synthesized oligodeoxyribonucleotide blocks. The oligodeoxyribonucleotides were prepared by the phosphoramidate method. Blocks (30-50 bases) were assembled by combining each phosphorylated component with equimolar amts. of the unphosphorylated oligomers from the complementary strand. Plasmid vectors were then used to clone the synthetic DNA fragments into the IFN-β-coding region. The vectors also contained the Escherichia coli trp promoter. The IFN-β formed by E. coli (IFNX414) had in vitro antiviral and antiproliferative activities .apprx.5-fold higher than those of IFN-β. Another recombinant IFN-β, IFNX401 had identical antiviral and immunostimulating activity to IFN-β but is 3 times more potent in its antiproliferative activity. Other group I IFNs prepared and characterized were IFNX412, 413, 421, and modified β-.

L18 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1984:4461 CAPLUS

DOCUMENT NUMBER: 100:4461

TITLE: A new mass-spectrometric C-terminal sequencing technique finds a similarity between γ-interferon and α2-interferon and identifies a proteolytically clipped γ-interferon that retains full antiviral activity

AUTHOR(S): Rose, Keith; Simona, Marco G.; Offord, Robin E.; Prior, Christopher P.; Otto, Berndt; Thatcher, David R.

CORPORATE SOURCE: Dep. Biochim., Cent. Med. Univ., Geneva, 1211/4, Switz.

SOURCE: Biochemical Journal (1983), 215(2), 273-7
CODEN: BIJOAK; ISSN: 0306-3275

DOCUMENT TYPE: Journal

LANGUAGE: English

AB During peptide sequence mapping, it is difficult to obtain sequence information from the C-terminus ; it is much easier to obtain sequence information from the N-terminus of a protein (Rose, K., et al, 1983). A novel mass-spectrometric technique is described here which permits identification of the C-terminal peptide of a protein. This technique involves the incorporation of 18O into all α-carboxy groups liberated during enzyme-catalyzed partial hydrolysis of the protein, followed by mass spectrometry to identify as the C-terminal peptide the only peptide that did not incorporate any 18O. This technique was used to identify the true C-terminal tryptic peptide of a bacterially-produced (recombinant technol.) γ-interferon (human) and to distinguish it from a peptide produced by an anomalous tryptic cleavage. A closely similar sequence segment of bacterially produced α2-interferon undergoes an analogous cleavage. The C-terminus of a clipped γ-interferon that retains full antiviral activity also was identified by using the technique.

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FILE 'MEDLINE' ENTERED AT 15:07:03 ON 25 MAR 2007

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                                                   ENTRY    SESSION
CA SUBSCRIBER PRICE                                -21.84     -21.84

=> D Hist

     (FILE 'HOME' ENTERED AT 13:34:30 ON 25 MAR 2007)

     FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE' ENTERED AT 13:34:48 ON 25 MAR 2007
L1         70256 S (INTERFERON ALPHA) OR IFN-ALPHA AND (MUTEIN OR VARIANT OR MUT
L2           248 S L1 AND PROTEOL?
L3           142 DUP REM L2 (106 DUPLICATES REMOVED)
L4            21 S L3 AND RESISTANCE
L5          2141 S L1 AND (IFN -ALPHA 2B)
L6             7 S L5 AND PROTEOL?
L7             3 DUP REM L6 (4 DUPLICATES REMOVED)
L8            21 S L5 AND GLYCOSYL?
L9            12 DUP REM L8 (9 DUPLICATES REMOVED)
L10            0 S L1 AND ((INCREASED ACTIVITY)(S)ANTIVIRAL)
L11            0 S L1 AND ((INCREASED ACTIVITY)(S)ANTI-PROLIFERATIVE)
L12         3560 S L1 AND  (ACTIVITY(S)ANTIVIRAL)
L13           93 S L1 AND (ACTIVITY(S)ANTI-PROLIFERATIVE)
L14         2040 DUP REM L12 (1520 DUPLICATES REMOVED)
L15           71 S L14 AND ((IFN-ALPHA 2B) OR IFNALPHA-2B)
L16            3 S L13 AND ((IFN-ALPHA 2B) OR IFNALPHA-2B)
L17            2 DUP REM L16 (1 DUPLICATE REMOVED)
L18           15 S L14 AND PROTEOL?

=> S L1(P)Protease
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L1(P)PROTEASE'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L2(P)PROTEASE'
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PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L3(P)PROTEASE'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L4(P)PROTEASE'
L19         837 L1(P) PROTEASE

=> Dup Rem L19
PROCESSING COMPLETED FOR L19
L20          588 DUP REM L19 (249 DUPLICATES REMOVED)

=> D Ti

L20  ANSWER 1 OF 588  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Preparation of spiroisoxazoline-based peptidomimetics as inhibitors of
     serine proteases, particularly HCV NS3-NS4A protease


=> S ((INTERFERON ALPHA) OR IFN-ALPHA)(P)protease
L21         547 ((INTERFERON ALPHA) OR IFN-ALPHA)(P) PROTEASE

=> S L21 AND pd<=20020909
L22         290 L21 AND PD<=20020909

=> Dup Rem L22
PROCESSING COMPLETED FOR L22
L23          136 DUP REM L22 (154 DUPLICATES REMOVED)

=> D Ti 1-5

L23  ANSWER 1 OF 136  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on
     STN
TI   AIDS-related Kaposi's sarcoma with chylothorax and pericardial involvement
     satisfactorily treated with liposomal doxorubicin.

L23  ANSWER 2 OF 136  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Preparation of recombinant protein as chaperon fusion protein

L23  ANSWER 3 OF 136  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Adhesion protein, protease, and protease inhibitor mutations and methods
     for diagnosis and treatment of epithelial cell adhesion-associated
     diseases

L23  ANSWER 4 OF 136  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Preparation of peptidomimetic protease inhibitors

L23  ANSWER 5 OF 136  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Preparation of novel peptides as NS3-serine protease inhibitors of
     hepatitis C virus


=> D Ti 1-136

L23  ANSWER 1 OF 136  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on
     STN
TI   AIDS-related Kaposi's sarcoma with chylothorax and pericardial involvement
     satisfactorily treated with liposomal doxorubicin.

L23  ANSWER 2 OF 136  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Preparation of recombinant protein as chaperon fusion protein

L23  ANSWER 3 OF 136  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Adhesion protein, protease, and protease inhibitor mutations and methods
```

for diagnosis and treatment of epithelial cell adhesion-associated diseases

L23 ANSWER 4 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of peptidomimetic protease inhibitors

L23 ANSWER 5 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of novel peptides as NS3-serine protease inhibitors of hepatitis C virus

L23 ANSWER 6 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Novel peptides as ns3-serine protease inhibitors of hepatitis C virus

L23 ANSWER 7 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of novel imidazolidinones as NS3-serine protease inhibitors of hepatitis C virus

L23 ANSWER 8 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of novel peptides as NS3-serine protease inhibitors of hepatitis C virus

L23 ANSWER 9 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI HIV/HCV co-infection: Clinical and therapeutic challenges.

L23 ANSWER 10 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Azapeptides as inhibitors of the Hepatitis C virus NS3 serine protease.

L23 ANSWER 11 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1
TI New therapies for the treatment of chronic hepatitis C

L23 ANSWER 12 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Ambroxol suppresses influenza-virus proliferation in the mouse airway by increasing antiviral factor levels.

L23 ANSWER 13 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 2
TI Treatment of hepatitis C.
Original Title: Traitement de l'hepatite C.

L23 ANSWER 14 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Adverse drug reaction update.

L23 ANSWER 15 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Proteolytic degradation of the recombinant target protein, interferon-τ during its fermentative production in the methylotrophic yeast, Pichia pastoris

L23 ANSWER 16 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 3
TI Management of protease inhibitor-associated hyperlipidemia

L23 ANSWER 17 OF 136 MEDLINE on STN
TI Monitoring of endogenous interferon-alpha and human herpesvirus 8 in HIV-infected patients with Kaposi's sarcoma.

L23 ANSWER 18 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of macrocyclic NS3-serine protease inhibitors of hepatitis C virus comprising n-cyclic p2 moieties

L23 ANSWER 19 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of peptides as inhibitors of serine proteases, particularly hepatitis C virus NS3 protease

L23 ANSWER 20 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Efficacy of cidofovir on human herpesvirus 8 viraemia and Kaposi's sarcoma progression in two patients with AIDS.

L23 ANSWER 21 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 4
TI Experimental and emerging therapies for chronic hepatitis C virus infection

L23 ANSWER 22 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 5
TI Prolonging the half-life of human interferon-α2 in circulation: design, preparation, and analysis of (2-sulfo-9-fluorenylmethoxycarbonyl)7-interferon-α2

L23 ANSWER 23 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Analysis of cytokine and chemokine related gene expression in peripheral blood mononuclear cells from lupus patients by DNA microarrays.

L23 ANSWER 24 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Treatment of hepatitis.

L23 ANSWER 25 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 6
TI Treatment with interferon-alpha (IFNalpha) of hepatitis C patients induces lower serum dipeptidyl peptidase IV activity, which is related to IFNalpha-induced depressive and anxiety symptoms and immune activation.

L23 ANSWER 26 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Constraints on hepatitis C virus (HCV) NS3 serine protease genetic heterogeneity and evolution.

L23 ANSWER 27 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Hepatitis C: An update.

L23 ANSWER 28 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 7
TI Angiogenesis: Regulators and clinical applications.

L23 ANSWER 29 OF 136 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
TI Hepatitis C: Therapeutic perspectives.

L23 ANSWER 30 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 8
TI Lowered serum dipeptidyl peptidase IV activity is associated with depressive symptoms and cytokine production in cancer patients receiving interleukin-2-based immunotherapy.

L23 ANSWER 31 OF 136 MEDLINE on STN
TI Current and future treatment of hepatitis C.

L23 ANSWER 32 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 9
TI Activation of caspase-3 in renal cell carcinoma cells by anthracyclines or

5-fluorouracil.

L23 ANSWER 33 OF 136 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
TI Current and future treatment of hepatitis C.

L23 ANSWER 34 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Aggressive daily interferon therapy in HIV-HCV coinfected patients.

L23 ANSWER 35 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Therapeutic uses of protease inhibitors to modulate cellular pathways and immunity

L23 ANSWER 36 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI RNase-L-dependent destabilization of interferon-induced mRNAs. A role for the 2-5A system in attenuation of the interferon response

L23 ANSWER 37 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Lack of interference between ribavirin and nucleosidic analogues in HIV/HCV co-infected individuals undergoing concomitant antiretroviral and anti-HCV combination therapy

L23 ANSWER 38 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 10
TI Localization of a receptor nonapeptide with a possible role in the binding of the type I interferons.

L23 ANSWER 39 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 11
TI Response-adjusted α-interferon therapy for chronic hepatitis C in HIV-infected patients

L23 ANSWER 40 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Lowered Serum Dipeptidyl Peptidase IV Activity is Associated with Depressive Symptoms and Cytokine Production in Cancer Patients Receiving Interleukin-2-Based Immunotherapy

L23 ANSWER 41 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Discoveries of novel biological means of controlling HIV and HIV disease

L23 ANSWER 42 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 12
TI NS3•4A protease as a target for interfering with hepatitis C virus replication

L23 ANSWER 43 OF 136 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
TI [Coinfection with the hepatitis C virus and HIV: Current aspects]. CO-INFECTION PAR LE VIRUS DE L'HEPATITE C ET LE VIRUS DE L'IMMUNODEFICIENCE HUMAINE: ASPECTS ACTUELS.

L23 ANSWER 44 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 13
TI Recent advances in the knowledge of biology and treatment of mastocytosis

L23 ANSWER 45 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Suppression of hepatitis C virus in human immunodeficiency virus iron-loading anemia (HCV-HIV-ILA) patients with HAART and recombinant human erythropoietin (r-HuEPO).

L23 ANSWER 46 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI STAT1 plays a protective role against the neurotoxic actions of chronic

IFN-alpha production in the CNS.

L23 ANSWER 47 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Plasma platelet-activating factor acetylhydrolase activity in human immunodeficiency virus infection and the acquired immunodeficiency syndrome

L23 ANSWER 48 OF 136 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN DUPLICATE 14
TI Current and evolving therapies for hepatitis C.

L23 ANSWER 49 OF 136 MEDLINE on STN
TI Overview of interferon therapy for chronic hepatitis C.

L23 ANSWER 50 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 15
TI Hepatitis C virus: current understanding and prospects for future therapies

L23 ANSWER 51 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 16
TI Active anti-interferon-alpha immunization: A European-Israeli, randomized, double-blind, placebo-controlled clinical trial in 242 HIV-1-infected patients (the EURIS study).

L23 ANSWER 52 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Inflammatory mediators regulate cathepsin S in macrophages and microglia: A role in attenuating heparan sulfate interactions.

L23 ANSWER 53 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 17
TI A new contained human immunodeficiency virus type 1 host cell system for evaluation of antiviral activities of interferons and other agents in vitro.

L23 ANSWER 54 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 18
TI Systemic mastocytosis. Recent advances in diagnosis and treatment.

L23 ANSWER 55 OF 136 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN DUPLICATE 19
TI Hepatitis c virus and human immunodeficiency virus: Clinical issues in coinfection.

L23 ANSWER 56 OF 136 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
TI Production of cytokines and metalloproteinases in rheumatoid synovitis is T cell dependent.

L23 ANSWER 57 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 20
TI Decrease of enhanced interferon alpha levels in sera of HIV-infected and AIDS patients receiving combined antiretroviral therapy.

L23 ANSWER 58 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 21
TI Treatment strategies for chronic hepatitis C: Update since the 1997 National Institutes of Health Consensus Development Conference.

L23 ANSWER 59 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Antivirals for hepatitis C virus: Challenges and prospects.

L23 ANSWER 60 OF 136 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
TI Treatment strategies for chronic hepatitis C: Update since the 1997 national institutes of health consensus development Conference.

L23 ANSWER 61 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Protease inhibitor and triple-drug therapy: cellular immune parameters are not restored in pediatric AIDS patients after 6 months of treatment

L23 ANSWER 62 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 22
TI Highly active antiretroviral therapy significantly improves the prognosis of patients with HIV-associated progressive multifocal leukoencephalopathy.

L23 ANSWER 63 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 23
TI Autocrine self-elimination of cultured ovarian cancer cells by tumor necrosis factor α (TNF-α)

L23 ANSWER 64 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 24
TI Regulation of the human protein C inhibitor gene expression in HepG2 cells: Role of Sp1 and AP2.

L23 ANSWER 65 OF 136 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
TI Mastocytosis.

L23 ANSWER 66 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 25
TI Hepatitis B and C viruses: molecular identification and targeted antiviral therapies

L23 ANSWER 67 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI alphaIFN and HIV-1 protease inhibitors (PI) inhibit HIV-8 infection: Possible therapeutic approaches for Kaposi's Sarcoma (KS).

L23 ANSWER 68 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Mechanism for differential induction of apoptosis by type I interferons.

L23 ANSWER 69 OF 136 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
TI Acquired immunodeficiency syndrome-associated Kaposi's sarcoma.

L23 ANSWER 70 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 26
TI Pharmacokinetic studies with recombinant cytokines. Scientific issues and practical considerations

L23 ANSWER 71 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 27
TI Obstruction of HIV-1 particle release by interferon-. alpha. occurs before viral protease processing and is independent of envelope glycoprotein

L23 ANSWER 72 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Obstruction of HIV-1 particle release by interferon-alpha occurs before viral protease processing and is independent of envelope glycoprotein.

L23 ANSWER 73 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on

STN DUPLICATE 28
TI Inhibition of replication of HIV in primary monocyte/macrophages by different antiviral drugs and comparative efficacy in lymphocytes.

L23 ANSWER 74 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 29
TI A new method of "in-cell reverse transcriptase-polymerase chain reaction" for the detection of BCR/ABL transcript in chronic myeloid leukemia patients.

L23 ANSWER 75 OF 136 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
TI The role of neutrophils as mediators.

L23 ANSWER 76 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 30
TI Induction of interleukin-6 by interferon alfa and its abrogation by a serine protease inhibitor in patients with chronic hepatitis C.

L23 ANSWER 77 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 31
TI A phase II study of interferon-alpha, interleukin-2 and 5-fluorouracil in advanced renal carcinoma: Clinical data and laboratory evidence of protease activation.

L23 ANSWER 78 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Suppression of UV- and interferon-α-refractoriness by antipain in human IFr cells established from RSa cells sensitive to both stimuli

L23 ANSWER 79 OF 136 MEDLINE on STN
TI Five-drug or six-drug antiretroviral therapy--conversation with Steven Scheibel, M.D. Interview by John S. James.

L23 ANSWER 80 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Suppression of saccharin-induced mutagenicity by interferon-α in human RSa cells

L23 ANSWER 81 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 32
TI Analysis of heterogeneity of gene products (interferon) expressed in yeast.

L23 ANSWER 82 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 33
TI In vitro inhibition of human immunodeficiency virus type 1 by a combination of delavirdine (U-90152) with protease inhibitor U-75875 or interferon-alpha.

L23 ANSWER 83 OF 136 MEDLINE on STN
TI Immune-based therapies.

L23 ANSWER 84 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 34
TI Inhibition of human immunodeficiency virus type 1 replication in cytokine-stimulated monocytes/macrophages by combination therapy.

L23 ANSWER 85 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 35
TI Crystal structure of the extracellular region of human tissue factor.

L23 ANSWER 86 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 36

TI Combination therapy for infection due to human immunodeficiency virus type 1.

L23 ANSWER 87 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Combination of peptide protease inhibitor and recombinant interferon-alpha A synergistically inhibited acute and chronic HIV-1 infection in vitro.

L23 ANSWER 88 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 37
TI In vitro activity of inhibitors of late stages of the replication of HIV in chronically infected macrophages.

L23 ANSWER 89 OF 136 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN DUPLICATE 38
TI Analysis of mast cell subpopulations (MC(T), MC(TC)) in cutaneous inflammation using novel enzyme-histochemical staining techniques.

L23 ANSWER 90 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Structure and physicochemical properties of purified human leukocyte interferon (FPI-31)

L23 ANSWER 91 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Interferon-alpha induces plasma interleukin-6 elevation in patients with chronic hepatitis C: Its abrogation by a serine protease inhibitor.

L23 ANSWER 92 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 39
TI Involvement of antipain-sensitive protease activity in suppression of UV-mutagenicity by human interferon-alpha .

L23 ANSWER 93 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 40
TI A stress-regulated protein, GRP58, a member of thioredoxin superfamily, is a carnitine palmitoyltransferase isoenzyme.

L23 ANSWER 94 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Inhibition of HIV-1 replication by convergent combination therapy in monocyte/macrophages.

L23 ANSWER 95 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 41
TI Regulation of neutrophil-derived IL-8: The role of prostaglandin E-2, dexamethasone, and IL-4.

L23 ANSWER 96 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 42
TI Inhibition of the protease of human immunodeficiency virus blocks replication and infectivity of the virus in chronically infected macrophages.

L23 ANSWER 97 OF 136 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
TI New antiretroviral agents for the therapy of HIV type-1 infection.

L23 ANSWER 98 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 43
TI Damage of tracer erythropoietin results in erroneous estimation of

concentration in mouse submaxillary gland

L23 ANSWER 99 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 44
TI Duplication of secretion signal sequences is deleterious for the secretion of human interferon α4 from Saccharomyces cerevisiae and Bacillus subtilis

L23 ANSWER 100 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 45
TI Inhibition of antigen-induced secretion in the rat jejunum by interferon alpha/beta.

L23 ANSWER 101 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI In vitro processing of fusion proteins

L23 ANSWER 102 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 46
TI Human immunodeficiency virus type 1 (HIV-1) inhibitory interactions between protease inhibitor Ro 31-8959 and zidovudine, 2' 3'-dideoxycytidine, or recombinant interferon-alpha A against zidovudine-sensitive or -resistant HIV-1 in vitro.

L23 ANSWER 103 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 47
TI FAT-STORING CELLS OF THE RAT LIVER SYNTHESIZE AND SECRETE C1 ESTERASE INHIBITOR MODULATION BY CYTOKINES.

L23 ANSWER 104 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 48
TI DIFFERENTIAL INACTIVATION OF INTERFERONS BY A PROTEASE FROM HUMAN GRANULOCYTES.

L23 ANSWER 105 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 49
TI Rapid high level production and purification of recombinant murine and human interferons alpha from Escherichia coli.

L23 ANSWER 106 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 50
TI DIFFERENTIAL MODULATION OF TWO INTERFERON-ALPHA BINDING PROTEINS ON A HUMAN LYMPHOBLASTOID CELL LINE.

L23 ANSWER 107 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 51
TI INTERFERON INHIBITOR IN THE BLOOD OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS.

L23 ANSWER 108 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Glycosylated polypeptides for better thermostability and protease resistance

L23 ANSWER 109 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 52
TI STRUCTURAL DESIGN AND MOLECULAR EVOLUTION OF A CYTOKINE RECEPTOR SUPERFAMILY.

L23 ANSWER 110 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 53
TI INTERFERON GAMMA INCREASES IN-VITRO AND IN-VIVO EXPRESSION OF C1 INHIBITOR.

L23 ANSWER 111 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on

STN DUPLICATE 54
TI A SENSITIVE TWO-SITE ENZYME IMMUNOASSAY FOR THE DETECTION OF RAT INTERFERON-GAMMA IN BIOLOGICAL FLUIDS.

L23 ANSWER 112 OF 136 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN DUPLICATE 55
TI Virologic and immunologic aspects of acquired immunodeficiency syndrome.

L23 ANSWER 113 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Identification of actinophage VWB promoters and their use for expression of murine interferon alpha in Streptomyces venezuelae and S. lividans

L23 ANSWER 114 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Inhibition of human natural killer cell activity by Legionella pneumophila protease

L23 ANSWER 115 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 56
TI SECRETORY EXPRESSION IN ESCHERICHIA-COLI AND BACILLUS-SUBTILIS OF HUMAN INTERFERON ALPHA GENES DIRECTED BY STAPHYLOKINASE SIGNALS.

L23 ANSWER 116 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 57
TI Mass spectrometric analysis of recombinant human α-2 interferon

L23 ANSWER 117 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 58
TI LOW TEMPERATURES STABILIZE INTERFERON ALPHA-2 AGAINST PROTEOLYSIS IN METHYLOPHILUS-METHYLOTROPHUS AND ESCHERICHIA-COLI.

L23 ANSWER 118 OF 136 MEDLINE on STN
TI [Monocyte-endothelium relations].
Relations monocytes-endothelium.

L23 ANSWER 119 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 59
TI CYTOSTATIC PRODUCTS RELEASED BY ACTIVATED MACROPHAGES UNRELATED TO INTERLEUKIN 1 TUMOR NECROSIS FACTOR ALPHA AND INTERFERON-ALPHA-BETA.

L23 ANSWER 120 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 60
TI SELECTIVE INDUCTION OF MONONUCLEAR PHAGOCYTES TO PRODUCE NEOPTERIN BY INTERFERONS.

L23 ANSWER 121 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 61
TI THE STABILITY OF NORMAL ABNORMAL AND GENETICALLY-ENGINEERED PROTEINS IN ESCHERICHIA-COLI STRAINS DEFICIENT IN THE LON-GENE PRODUCTS INTRACELLULAR PROTEASE LA.

L23 ANSWER 122 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Plasmids which include promoters for bacteriocins adapted for expression of foreign polypeptides in Escherichia coli

L23 ANSWER 123 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Identification and partial characterization of a novel protease in Saccharomyces cerevisiae which cleaves the peptide bond between residues 22 and 23 in α-interferon, and identification of an α-interferon resistant to said proteolysis

L23 ANSWER 124 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 62
TI INTERFERON-GAMMA IS A MAJOR REGULATOR OF C1-INHIBITOR SYNTHESIS BY HUMAN

BLOOD MONOCYTES.

L23 ANSWER 125 OF 136 MEDLINE on STN
TI Production and function of the monocyte cytotoxic factor (MCF).

L23 ANSWER 126 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 63
TI HUMAN MONOCYTE OR RECOMBINANT INTERLEUKIN 1'S ARE SPECIFIC FOR THE SECRETION OF A METALLOPROTEINASE FROM CHONDROCYTES.

L23 ANSWER 127 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 64
TI INTRACELLULAR DEGRADATION OF RECOMBINANT PROTEINS IN RELATION TO THEIR LOCATION IN ESCHERICHIA-COLI CELLS.

L23 ANSWER 128 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 65
TI HUMAN INTERFERON GAMMA INCREASES ADHESION OF CULTURED CARCINOMA CELLS TO THE SUBSTRATUM.

L23 ANSWER 129 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 66
TI A LYMPHOKINE REGULATES EXPRESSION OF ALPHA-1 PROTEINASE INHIBITOR IN HUMAN MONOCYTES AND MACROPHAGES.

L23 ANSWER 130 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Secretion of mature IFN-α2 and accumulation of uncleaved precursor by Bacillus subtilis transformed with a hybrid α-amylase signal sequence-IFN-α2 gene

L23 ANSWER 131 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI An interferon-like activity released by human peripheral blood mononuclear cells treated with inhibitors of transcription: a new type of interferon?

L23 ANSWER 132 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Interferon administration vehicles

L23 ANSWER 133 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 67
TI MONOCLONAL ANTIBODIES ELECTROPHORETICALLY TRANSFERRED FROM POLYACRYLAMIDE GELS RETAIN THEIR ABILITY TO BIND SPECIFIC ANTIGENS.

L23 ANSWER 134 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 68
TI ENZYME IMMUNOASSAY OF HUMAN INTERFERON-ALPHA USING MONOCLONAL ANTIBODY.

L23 ANSWER 135 OF 136 MEDLINE on STN
TI Interferon is a polypeptide hormone.

L23 ANSWER 136 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 69
TI REDUCED SYNTHESIS OF PP-60 S-R-C AND EXPRESSION OF THE TRANSFORMATION RELATED PHENOTYPE IN INTERFERON TREATED ROUS SARCOMA VIRUS TRANSFORMED RAT CELLS.

=> S L23 AND (Interferon-alpha 2b)
L24 5 L23 AND (INTERFERON-ALPHA 2B)

=> D Ti 1-5

L24 ANSWER 1 OF 5 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

```
TI   Treatment of hepatitis.

L24  ANSWER 2 OF 5  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
TI   Treatment strategies for chronic hepatitis C: Update since the 1997
     National Institutes of Health Consensus Development Conference.

L24  ANSWER 3 OF 5  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Preparation of recombinant protein as chaperon fusion protein

L24  ANSWER 4 OF 5  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Preparation of peptidomimetic protease inhibitors

L24  ANSWER 5 OF 5  EMBASE  COPYRIGHT (c) 2007 Elsevier B.V. All rights
     reserved on STN
TI   Mastocytosis.


=> Loggoff h
LOGGOFF IS NOT A RECOGNIZED COMMAND
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=> log off h
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SESSION RESUMED IN FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE'
AT 16:09:18 ON 25 MAR 2007
FILE 'BIOSIS' ENTERED AT 16:09:18 ON 25 MAR 2007
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FILE 'MEDLINE' ENTERED AT 16:09:18 ON 25 MAR 2007

COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
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FULL ESTIMATED COST 340.59 340.80

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE ENTRY TOTAL SESSION
CA SUBSCRIBER PRICE -26.52 -26.52

=> D Hist

(FILE 'HOME' ENTERED AT 13:34:30 ON 25 MAR 2007)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE' ENTERED AT 13:34:48 ON 25 MAR 2007
L1 70256 S (INTERFERON ALPHA) OR IFN-ALPHA AND (MUTEIN OR VARIANT OR MUT
L2 248 S L1 AND PROTEOL?
L3 142 DUP REM L2 (106 DUPLICATES REMOVED)
L4 21 S L3 AND RESISTANCE
L5 2141 S L1 AND (IFN -ALPHA 2B)
L6 7 S L5 AND PROTEOL?
L7 3 DUP REM L6 (4 DUPLICATES REMOVED)
L8 21 S L5 AND GLYCOSYL?
L9 12 DUP REM L8 (9 DUPLICATES REMOVED)
L10 0 S L1 AND ((INCREASED ACTIVITY)(S)ANTIVIRAL)
L11 0 S L1 AND ((INCREASED ACTIVITY)(S)ANTI-PROLIFERATIVE)
L12 3560 S L1 AND (ACTIVITY(S)ANTIVIRAL)
L13 93 S L1 AND (ACTIVITY(S)ANTI-PROLIFERATIVE)
L14 2040 DUP REM L12 (1520 DUPLICATES REMOVED)
L15 71 S L14 AND ((IFN-ALPHA 2B) OR IFNALPHA-2B)
L16 3 S L13 AND ((IFN-ALPHA 2B) OR IFNALPHA-2B)
L17 2 DUP REM L16 (1 DUPLICATE REMOVED)
L18 15 S L14 AND PROTEOL?
L19 837 S L1(P)PROTEASE
L20 588 DUP REM L19 (249 DUPLICATES REMOVED)
L21 547 S ((INTERFERON ALPHA) OR IFN-ALPHA)(P)PROTEASE
L22 290 S L21 AND PD<=20020909
L23 136 DUP REM L22 (154 DUPLICATES REMOVED)
L24 5 S L23 AND (INTERFERON-ALPHA 2B)

=> D L23 Ibib Abs 108, 116, 123

L23 ANSWER 108 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1991:137408 CAPLUS
DOCUMENT NUMBER: 114:137408
TITLE: Glycosylated polypeptides for better thermostability and protease resistance
INVENTOR(S): Sasaki, Katsutoshi; Nishi, Tatsunari; Yasumura, Shigeyoshi; Sato, Moriyuki; Itoh, Seiga
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 130 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 370205	A2	19900530	EP 1989-117981	19890928 <--
EP 370205	A3	19900613		
EP 370205	B1	19980722		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5218092	A	19930608	US 1989-413482	19890927 <--
JP 02227075	A	19900910	JP 1989-253097	19890928 <--
JP 2928287	B2	19990803		

AT 168699	T	19980815	AT 1989-117981	19890928	<--
ES 2121734	T3	19981216	ES 1989-117981	19890928	<--
CA 1341385	C	20020820	CA 1989-614003	19890928	<--

PRIORITY APPLN. INFO.: JP 1988-245705 A 19880929

AB Physiol. active polypeptide-encoding gene is mutagenized such that ≥1 new glycosylation sites (markush structure given) are formed. The gene is introduced by transformation into, e.g. CHO cells, to produce glycosylated physiol. active polypeptides, e.g. urokinase, containing ≥1 new carbohydrate chains. Plasmid pAS28 encoding glycosylated human granulocyte colony stimulating factor hG-CSF[ND28] was constructed and introduced into CHO cells for production The recombinant hG-CSF[ND28] was a mixture of singly and doubly O-glycosylated froms. The recombinant hG-CSF[ND28] mixture had a better protease-resistance than that of the wild type hG-CSF; and hG-CSF[ND28] having 2 carbohydrate chains had better protease-resistance than that having only one. Glycosylated hG-CSF, hG-CSF[ND28N6], had better thermostability at 56° than the nonglycosylated counterpart obtained by N-glycanase treatment. Glycosylated urokinase, similarly, was prepared. Like natural prourokinase, it scarcely activated the systemic fibrinolytic system; and it had less sensitivity to thrombin and a prolonged plasma elimination half-life (.apprx.2-fold).

L23 ANSWER 116 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 57

ACCESSION NUMBER:	1989:590765 CAPLUS
DOCUMENT NUMBER:	111:190765
TITLE:	Mass spectrometric analysis of recombinant human α-2 interferon
AUTHOR(S):	Padron, G.; Besada, V.; Agraz, A.; Quinones, Y.; Herrera, L.; Shimonishi, Y.; Takao, T.
CORPORATE SOURCE:	Cent. Genet. Eng. Biotechnol., Havana, Cuba
SOURCE:	Analytica Chimica Acta (1989), 223(2), 361-9 CODEN: ACACAM; ISSN: 0003-2670
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Mass spectrometry (MS) was used for the characterization of recombinant human α-2 interferon (α -2 IFN) produced in Escherichia coli. After purification by monoclonal antibody affinity chromatog., α-2 IFN showed two major peaks in reversed-phase liquid chromatog. (RP-LC). Each component was digested with trypsin and Staphylococcus aureus protease V8, sep. or in tandem, and the peptide mixture was analyzed by MS without further purification The first peak corresponded to the 165 amino acid sequence of human α-2 IFN and the main component of the second peak was the acetylated Cys1 α-2 IFN. It was also possible to verify by MS the location of the S-S bonds in α-2 IFN and the occurrence of incorrect S-S bridges in the products of some renaturation processes. The best renaturation process for obtaining a product without adducts or scrambling of disulfide bonds could be found by using RP-LC and fast-atom-bombardment MS.

L23 ANSWER 123 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	1988:144742 CAPLUS
DOCUMENT NUMBER:	108:144742
TITLE:	Identification and partial characterization of a novel protease in Saccharomyces cerevisiae which cleaves the peptide bond between residues 22 and 23 in α-interferon, and identification of an α-interferon resistant to said proteolysis
INVENTOR(S):	O'Loughlin, John T.
PATENT ASSIGNEE(S):	Interferon Sciences, Inc., USA
SOURCE:	Eur. Pat. Appl., 20 pp. CODEN: EPXXDW
DOCUMENT TYPE:	Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 240224	A2	19871007	EP 1987-302519	19870324 <--
EP 240224	A3	19890201		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DK 8701614	A	19871001	DK 1987-1614	19870330 <--
CN 87102497	A	19871111	CN 1987-102497	19870330 <--
JP 62296892	A	19871224	JP 1987-74566	19870330 <--

PRIORITY APPLN. INFO.: US 1986-845937 A 19860331

AB A novel S. cerevisiae protease cleaves α-interferons between basic amino acids at positions 22 and 23, but cleavage does not occur if residue 22 is serine. A recombinant interferon . alpha. with serine, threonine, asparagine, glutamine, or glycine at position 22 could be produced intact in a microorganism whose primary proteolytic activity against the natural species is at that site. The protease was partially purified. from a protease -deficient PEP 3-4 S. cerevisiae mutant. It was membrane-bound and activated by the Triton X-100 present during cell lysis. Recombinant interferons α -1, α-2, and α-8 were all incubated with the protease. Both α-2 and α-8 were cleaved between amino acids 22 and 23 (which were Arg-Lys and Arg-Arg, resp.), but α-1 (Ser-Arg) was not.

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AT 16:16:55 ON 25 MAR 2007
FILE 'BIOSIS' ENTERED AT 16:16:55 ON 25 MAR 2007

FILE 'CAPLUS' ENTERED AT 16:16:55 ON 25 MAR 2007

FILE 'EMBASE' ENTERED AT 16:16:55 ON 25 MAR 2007

FILE 'MEDLINE' ENTERED AT 16:16:55 ON 25 MAR 2007

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	350.02	350.23

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-28.86	-28.86

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STN INTERNATIONAL LOGOFF AT 16:17:09 ON 25 MAR 2007

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PASSWORD:
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NEWS 2	JUL 28	CA/CAplus patent coverage enhanced
NEWS 3	JUL 28	EPFULL enhanced with additional legal status information from the epoline Register
NEWS 4	JUL 28	IFICDB, IFIPAT, and IFIUDB reloaded with enhancements
NEWS 5	JUL 28	STN Viewer performance improved
NEWS 6	AUG 01	INPADOCDB and INPAFAMDB coverage enhanced
NEWS 7	AUG 13	CA/CAplus enhanced with printed Chemical Abstracts page images from 1967-1998
NEWS 8	AUG 15	CAOLD to be discontinued on December 31, 2008
NEWS 9	AUG 15	CAplus currency for Korean patents enhanced
NEWS 10	AUG 27	CAS definition of basic patents expanded to ensure comprehensive access to substance and sequence information
NEWS 11	SEP 18	Support for STN Express, Versions 6.01 and earlier, to be discontinued
NEWS 12	SEP 25	CA/CAplus current-awareness alert options enhanced to accommodate supplemental CAS indexing of exemplified prophetic substances
NEWS 13	SEP 26	WPIDS, WPINDEX, and WPIX coverage of Chinese and and Korean patents enhanced
NEWS 14	SEP 29	IFICLS enhanced with new super search field
NEWS 15	SEP 29	EMBASE and EMBAL enhanced with new search and display fields
NEWS 16	SEP 30	CAS patent coverage enhanced to include exemplified prophetic substances identified in new Japanese-language patents
NEWS 17	OCT 07	EPFULL enhanced with full implementation of EPC2000
NEWS 18	OCT 07	Multiple databases enhanced for more flexible patent number searching
NEWS 19	OCT 22	Current-awareness alert (SDI) setup and editing enhanced
NEWS 20	OCT 22	WPIDS, WPINDEX, and WPIX enhanced with Canadian PCT Applications
NEWS 21	OCT 24	CHEMLIST enhanced with intermediate list of pre-registered REACH substances

NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

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                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'MEDLINE' ENTERED AT 15:27:15 ON 04 NOV 2008

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=> S (Crystal structure) (S) (interferon alpha) AND pd<=20020606
   1 FILES SEARCHED...
L1          11 (CRYSTAL STRUCTURE) (S) (INTERFERON ALPHA) AND PD<=20020606

=> Dup Rem L1
PROCESSING COMPLETED FOR L1
L2             8 DUP REM L1 (3 DUPLICATES REMOVED)
                 ANSWERS '1-2' FROM FILE MEDLINE
                 ANSWER '3' FROM FILE BIOSIS
                 ANSWERS '4-7' FROM FILE CAPLUS
                 ANSWER '8' FROM FILE EMBASE

=> D Ibib abs L2 1-8

L2   ANSWER 1 OF 8     MEDLINE on STN                    DUPLICATE 2
ACCESSION NUMBER:   1997148339     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 8994971
TITLE:              Zinc mediated dimer of human interferon-alpha 2b revealed
                    by X-ray crystallography.
AUTHOR:             Radhakrishnan R; Walter L J; Hruza A; Reichert P; Trotta P
                    P; Nagabhushan T L; Walter M R
CORPORATE SOURCE:   Center for Macromolecular Crystallography, University of
                    Alabama at Brimingham 35294, USA.
CONTRACT NUMBER:    CA36871 (United States NCI)
                    NS29719 (United States NINDS)
SOURCE:             Structure (London, England : 1993), (1996 Dec 15)
                    Vol. 4, No. 12, pp. 1453-63.
                    Journal code: 101087697. ISSN: 0969-2126.
PUB. COUNTRY:       ENGLAND: United Kingdom
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
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(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 27 Mar 1997
Last Updated on STN: 27 Mar 1997
Entered Medline: 19 Mar 1997

AB BACKGROUND: The human alpha-interferon (huIFN-alpha) family displays broad spectrum antiviral, antiproliferative and immunomodulatory activities on a variety of cell types. The diverse biological activities of the IFN-alpha's are conveyed to cells through specific interactions with cell-surface receptors. Despite considerable effort, no crystal structure of a member of this family has yet been reported, because the quality of the protein crystals have been unsuitable for crystallographic studies. Until now, structural models of the IFN-alpha's have been based on the structure of murine IFN-beta (muIFN-beta). These models are likely to be inaccurate, as the amino acid sequence of muIFN-beta differs significantly from the IFN-alpha's at proposed receptor-binding sites. Structural information on a huIFN-alpha subtype would provide an improved basis for modeling the structures of the entire IFN-alpha family. RESULTS: The crystal structure of recombinant human interferon-alpha 2b (huIFN-alpha 2b) has been determined at 2.9 A resolution. HuIFN-alpha 2b exists in the crystal as a noncovalent dimer, which associates in a novel manner. Unlike other structurally characterized cytokines, extensive interactions in the dimer interface are mediated by a zinc ion (Zn2+). The overall fold of huIFN-alpha 2b is most similar to the structure of muIFN-beta. Unique to huIFN-alpha 2b is a 3(10) helix in the AB loop which is held to the core of the molecule by a disulfide bond. CONCLUSIONS: The structure of huIFN-alpha 2b provides an accurate model for analysis of the > 15 related type 1 interferon molecules. HuIFN-alpha 2b displays considerable structural similarity with muIFN-beta, interleukin-10 and interferon-gamma, which also bind related class 2 cytokine receptors. From these structural comparisons and numerous studies on the effects of mutations on biological activity, we have identified protein surfaces that appear to be important in receptor activation. This study also reveals the potential biological importance of the huIFN-alpha 2b dimer.

L2 ANSWER 2 OF 8 MEDLINE on STN
ACCESSION NUMBER: 19973524?8 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9208873
TITLE: Three-dimensional models of interferon-alpha subtypes IFN-con1, IFN-alpha8, andIFN-alpha1 derived from the crystal structure of IFN-alpha2b.
AUTHOR: Walter M R
CORPORATE SOURCE: Department of Pharmacology, University of Alabama at Birmingham, 35294-0005, USA.
CONTRACT NUMBER: AI36871-02 (United States NIAID)
P01 NS29719-05 (United States NINDS)
SOURCE: Seminars in oncology, (1997 Jun) Vol. 24, No. 3 Suppl 9, pp. S9-52-S9-62. Ref: 33
Journal code: 0420432. ISSN: 0093-7754.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707

ENTRY DATE: Entered STN: 24 Jul 1997
Last Updated on STN: 3 Mar 2000
Entered Medline: 15 Jul 1997

AB The crystal structure of human interferon (Hu-IFN)-alpha2b has been determined at 2.9 A resolution. This experimentally derived model provides an accurate structural scaffold on which amino acid changes between the different human IFN-alpha subtypes may be compared. Accurate structural data are essential to identify structurally important residues buried in the hydrophobic core of the molecule from solvent accessible residues that may participate in receptor binding. Furthermore, the location and chemical composition of each amino acid substitution may be used to predict potential conformation changes that may occur in the different subtypes. The possible structural and surface effects of these amino acid changes on receptor binding and biologic activity are analyzed in the context of a proposed IFN-alpha receptor complex model. This model can be improved and corrected as additional biochemical and experimental structural data are obtained. These modeling techniques have been used to assess the structural and functional consequences of amino acid changes between Hu-IFN-alpha2b and consensus IFN (IFN-con1), Hu-IFN-alpha8, and Hu-IFN-alpha1, which each have distinct receptor-binding and biologic properties. Amino acids in IFN-alpha1 and IFN-alpha8 were identified that may explain the lower specific activities of these subtypes versus the activity of IFN-alpha2b. In contrast, a molecular explanation for the reported differences between IFN-alpha2b in receptor binding affinity of either IFN-alpha8 or IFN-con1 was not readily apparent. Notably, 15 of the 19 amino acid differences in IFN-con1 compared with IFN-alpha2b are located on the exterior surface, where they may enhance the antigenicity of this synthetic, nonnaturally occurring IFN. These modeling studies should assist in the design of further experiments to clarify these observations.

L2 ANSWER 3 OF 8 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
DUPLICATE 1
ACCESSION NUMBER: 1997:368100 BIOSIS
DOCUMENT NUMBER: PREV199799667303
TITLE: Three-dimensional models of interferon-alpha subtypes IFN-conI, IFN-alpha-8, and IFN-alpha-1 derived from the crystal structure of IFN-alpha-2b.
AUTHOR(S): Walter, Mark R.
CORPORATE SOURCE: Dep. Pharmacol., Univ. Alabama at Birmingjam, 268 Basic Health Sci. Build., THT 79, 1918 University Blvd., Birmingham, AL 35294-0005, USA
SOURCE: Seminars in Oncology, (1997) Vol. 24, No. 3 SUPPL. 9, pp. 52-62.
CODEN: SOLGAV. ISSN: 0093-7754.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Sep 1997
Last Updated on STN: 4 Sep 1997

L2 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:4432 CAPLUS
DOCUMENT NUMBER: 130:221881
TITLE: Human interferon alpha 2b behaves as a trimer at basic pH. A preliminary x-ray diffraction analysis of human alpha interferon crystals grown at basic pH
AUTHOR(S): Diaz-Ruano, Aida; Segura-Nieto, Magdalena; Cuevas, Berenice; Prange, Thierry
CORPORATE SOURCE: Centro Ingenieria Genetica & Biotecnologia, Havana, Cuba
SOURCE: Biotecnologia Aplicada (1998), 15(4),

232-236
CODEN: BTAPEP; ISSN: 0864-4551
PUBLISHER: Sociedad Iberolatinoamericana de Biotecnologia Aplicada a la Salud
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Recombinant human α 2b interferon (hum alpha 2bIFN) was studied by sedimentation, gel filtration, and crosslinking experiences. These experiences showed that the quaternary structure of hum alpha 2bIFN changes at different pH. A preliminary x-ray anal. of low resolution orthorhombic crystals of this mol. was done and the crystallog. asym. unit contains 12 mols., possibly 4 trimers according to the previous sedimentation, gel filtration, and crosslinking experiences. The role of the Zn2+ ions in the stabilization of the quaternary structure of α interferon is discussed.

L2 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:130418 CAPLUS
DOCUMENT NUMBER: 126:203718
ORIGINAL REFERENCE NO.: 126:39306h,39307a
TITLE: Method for producing metal-interferon-α crystals for controlled-release pharmaceutical formulation
INVENTOR(S): Reichert, Paul; Mcnemar, Charles; Nagahhushan, Nagamani; Nagahhushan, Tattanahalli L.; Tindall, Stephen; Hruza, Alan
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: U.S., 10 pp., Cont.-in-part of U.S. 5, 441, 734. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5602232	A	19970211	US 1994-356021	19941214 <--
US 5441734	A	19950815	US 1993-24330	19930225 <--
CA 2156921	A1	19940901	CA 1994-2156921	19940224 <--
CN 1120846	A	19960417	CN 1994-191694	19940224 <--
HU 72973	A2	19960628	HU 1995-2485	19940224 <--
PRIORITY APPLN. INFO.:			US 1993-24330	A2 19930225

AB A method for producing a crystalline zinc interferon (IFN) α-2 is claimed comprising forming a soluble solution of IFN α-2 and a metal acetate salt under conditions wherein supersatn. and metal α-interferon crystals occur. Cobalt interferon α-2 is also crystallized Methods include liquid diffusion, vapor diffusion, and hanging drop techniques. The crystal structure and monoclinic morphol. of zinc IFN α-2 are characterized. Crystalline metal interferon-α is useful as a controlled-release pharmaceutical formulation.

L2 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1996:538106 CAPLUS
DOCUMENT NUMBER: 125:245277
ORIGINAL REFERENCE NO.: 125:45817a,45820a
TITLE: Refolding, isolation and characterization of crystallizable human interferon-α8 expressed in Saccharomyces cerevisiae
AUTHOR(S): Di Marco, Stefania; Fendrich, Gabriele; Meyhack, Bernd; Gruetter, Markus G.
CORPORATE SOURCE: Department of Core Drug Discovery Technology, Pharmaceuticals Division, Ciba-Geigy, Ltd., CH-4002, Basel, Switz.

SOURCE: Journal of Biotechnology (1996), 50(1), 63-73
CODEN: JBITD4; ISSN: 0168-1656
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Human interferon-α8 was expressed in S. cerevisiae and found to accumulate intracellularly in an insol. form. The protein could be solubilized and converted to a biol. active form with high yield by a denaturation-refolding procedure. The interferon-α8 was further purified to apparent homogeneity by copper-chelate affinity chromatog. and anion-exchange chromatog. and fully characterized by SDS-PAGE, N-terminal sequence anal., mass spectrometry, CD spectroscopy, and specific activity. Secondary-structure predictions from CD spectroscopy indicate that the mol. is correctly folded. Peptide mapping supported the correct sequence and the expected disulfide-bridge connectivity. The purified protein elutes on reversed-phase high-pressure liquid chromatog. (RP-HPLC) as 2 peaks. Electrospray mass spectrometry and N-terminal sequence anal. of the minor component indicated the existence of an N-terminal acetyl group for the later eluting HPLC-component. In anti-viral assays, the two IFN forms were equally active. Hexagonal crystals of this interferon preparation could be obtained. On the basis of the electrophoretic mobility, HPLC profile, and biol. activity assay, the crystalline material was judged to be identical to the uncrystd. interferon. Interferon in crystallized form was stable for up to 24 mo and, therefore, could be used for long-term storage, particularly for material intended for clin. use.

L2 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:623535 CAPLUS
DOCUMENT NUMBER: 119:223535
ORIGINAL REFERENCE NO.: 119:39849a,39852a
TITLE: Structural, functional and evolutionary implications of the three-dimensional crystal structure of murine interferon-β
AUTHOR(S): Mitsui, Yukio; Senda, Toshiya; Shimazu, Tsuneo; Matsuda, Susumu; Utsumi, Jun
CORPORATE SOURCE: Dep. BioEng., Nagaoka Univ. Technol., Nagaoka, 940-21, Japan
SOURCE: Pharmacology & Therapeutics (1993), 58(1), 93-132
CODEN: PHTHDT; ISSN: 0163-7258
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 187 refs. The crystal structure of recombinant murine interferon-β appears to represent the basic structural framework of all type I interferons including interferons-β and all subtypes of interferons-. alpha. of various mammalian origin. Now the accumulated data on the structure-activity relationship of type I interferons using various chemical and genetic techniques can be systematically evaluated in terms of the three-dimensional structure. Structural comparison with other cytokines, for which three-dimensional structures have been established, including interferon-γ and considerations on the evolution of cytokines and cytokine receptors are also given.

L2 ANSWER 8 OF 8 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 1997191327 EMBASE
TITLE: Three-dimensional models of interferon-. alpha. subtypes IFN-con1, IFN-α(8), and IFN-α(1) derived from the crystal structure of IFN-α(2b).

AUTHOR: Walter, M.R., Dr. (correspondence)
CORPORATE SOURCE: Department of Pharmacology, University of Alabama at Birmingham, 268 Basic Health Sciences Bldg, 1918 University Blvd, Birmingham, AL 35294-0005, United States.
SOURCE: Seminars in Oncology, (1997) Vol. 24, No. 3
SUPPL. 9, pp. S952-S962.
Refs: 33
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AB The crystal structure of human interferon (Hu-IFN)-α(2b) has been determined at 2.9 A resolution. This experimentally derived model provides an accurate structural scaffold on which amino acid changes between the different human IFN-α subtypes may be compared. Accurate structural data are essential to identify structurally important residues buried in the hydrophobic core of the molecule from solvent accessible residues that may participate in receptor binding. Furthermore, the location and chemical composition of each amino acid substitution may be used to predict potential conformation changes that may occur in the different subtypes. The possible structural and surface effects of these amino acid changes on receptor binding and biologic activity are analyzed in the context of a proposed IFN- α receptor complex model. This model can be improved and corrected as additional biochemical and experimental structural data are obtained. These modeling techniques have been used to assess the structural and functional consequences of amino acid changes between Hu-IFN-α(2b) and consensus IFN (IFN-conl), Hu-IFN-α(8), and Hu-IFN-α(1), which each have distinct receptor- binding and biologic properties. Amino acids in IFN-α(1) and IFN-α(8) were identified that may explain the lower specific activities of these subtypes versus the activity of IFN-α(2b). In contrast, a molecular explanation for the reported differences between IFN-α(2b) in receptor binding affinity of either IFN-α(8) or IFN-conl was not readily apparent. Notably, 15 of the 19 amino acid differences in IFN-conl compared with IFN-α(2b) are located on the exterior surface, where they may enhance the antigenicity of this synthetic, nonnaturally occurring IFN. These modeling studies should assist in the design of further experiments to clarify these observations.

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ACCESSION NUMBER:         1996:640775  CAPLUS
DOCUMENT NUMBER:          125:322475
ORIGINAL REFERENCE NO.:   125:60283a,60286a
TITLE:                    Fatal Sindbis virus infection of neonatal mice in the
                          absence of encephalitis
AUTHOR(S):                Trgovcich, Joanne; Aronson, Judith F.; Johnston,
                          Robert E.
CORPORATE SOURCE:         Dep. Microbiology and Immunology, Univ. North Carolina
                          Chapel Hill Schl. Med., Chapel Hill, NC, 27599-7290,
                          USA
SOURCE:                   Virology (1996), 224(1), 73-83
                          CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER:                Academic
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   A comparative pathogenesis study was performed in neonatal mice using a
     molecularly cloned laboratory variant of Sindbis strain AR339, designated TRSB,
     and a single-site attenuated mutant of TRSB derived by site-directed
     mutagenesis of the E2 glycoprotein from Ser to Arg at residue 114
     (TRSBr114).  TRSB caused 100% morality with an average survival time of
     3.0±0.7 days, whereas mice inoculated with TRSBr114 exhibited an
     attenuated disease course with 46% mortality and an extended average survival
     time of 7.5±3.4 days for those animals that died.  Reduced virulence of
     TRSBr114 was characterized by delayed appearance of detectable virus,
     relative to TRSB, and by lower peak virus titers in both sera and brains
     of infected mice.  TRSB infection induced very high peak serum titers of
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interferon alpha/beta (215,000 units/mL compared to 2100 units/mL for TRSBR114). In situ hybridization anal. demonstrated replication of TRSB in brain, but only minimal histopathol. changes and no evidence of encephalitis were observed However, extensive extraneural lesions and viral replication were found in skin, connective tissue, and muscle. Moreover, dramatic involution of the thymus and loss of hematopoietic tissues were observed in the absence of virus replication at these sites, suggesting the involvement of a systemic physiol. stress response in TRSB infection. TRSBr114 infection did not cause thymic lesions. Otherwise, the attenuated mutant demonstrated a similar pattern of tissue and organ involvement, but lesions and pos. in situ hybridization signal were much more limited in scope and intensity compared to TRSB. TRSBr114-infected mice developed myositis and encephalomyelitis approx. 6 days postinfection. Therefore, TRSB-infected animals may succumb to an early syndrome associated with the stress response, preventing their survival for a time sufficient for the development of encephalitis. Alternatively, a systemic stress response, as evidenced by thymic involution, may result in immunosuppression, thus contributing the the absence of encephalitis. In any event, the attenuation mutation in the E2 glycoprotein significantly altered the course of Sindbis-induced disease by limiting virus replication and associated damage early infection. Mutant-infected animals survived beyond Day 4 and progressed to a classical encephalomyelitis from which about half recovered.